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# The Effect of Thyroid and Thyroxine on Milk Secretion in Dairy Cattle

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# The Effect of Thyroid and Thyroxine on Milk Secretion in Dairy Cattle\*

H. A. HERMAN, W. R. GRAHAM, JR., and C. W. TURNER

Physiologists have long recognized that the secretion of the thyroid gland is responsible for the regulation of general body metabolism. Upon thyroidectomy there follows a marked reduction in the metabolic rate, whereas upon feeding thyroid or injecting thyroxine the metabolism may be considerably increased. However, the fact that the pituitary secreted a hormone (the thyrotropic factor) which regulates thyroid activity, has been a product of recent endocrine research.

Grimmer (1918) and Grimmer and Paul (1930) were first to observe that thyroidectomy was followed by a decline but not a cessation of milk secretion in goats. Grueter (1931) reported that the removal of the thyroid from goats soon after parturition caused a lowering of milk production to about one-half of what it was before the operation.

Graham (1934) was the first to report the results of extensive studies with thyroidectomized dairy cattle and with thyroid feeding of lactating cows. The diminution in milk secretion following removal of the thyroid could not be distinguished readily from that accompanying a control operation. However, when small amounts of dried thyroid glands were fed to either thyroidectomized or unoperated normal cows, when the latter were in the declining phase of lactation, there was a distinct rise in milk secretion. The feeding of excessive quantities of thyroid tissue, however, caused a decline in milk flow. That the stimulating factor in the thyroid gland was thyroxine was shown by an increase in milk secretion when synthetic thyroxine was injected (Graham, 1934). These observations have since been confirmed by Jack and Bechdel (1935) and Folley and White (1936). In the latter experiment 10 mg. daily of thyroxine for 15 days caused four Dairy Shorthorn cows in the declining phase of lactation to increase 28 per cent above the basal value in milk production and 50 per cent in fat production. It was noted that the pulse rate was increased 22 beats per minute. In this connection it is interesting to note that Fuller (1928) observed that high producing cows on a high plane of nutrition

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had appreciably higher pulse rates than cows producing at lower levels.

In the light of these studies it is significant that Reece and Turner (1937) observed a tendency for pituitaries from lactating cows to contain more of the thyrotropic hormone than those from dry cows. Furthermore on the basis of equal weight of pituitary tissue, the glands from dairy cows contained decidedly more of the thyrotropic hormone than those from beef cows.

There is increasing evidence that the pituitary and thyroid glands play an important role in the stimulation of milk secretion through the action of thyrotropic and thyroxine hormones. If the pituitary secreted optimum amounts of the thyrotropic hormone, it would be expected that the thyroid gland in turn would secrete optimum amounts of thyroxine for maximum milk secretion. However, the amount of thyroid tissue might be a limiting factor or the pituitary might secrete the thyrotropic hormone in insufficient amount. Cows with a genetic deficiency of either type would be expected to respond to the addition of thyroxine. It has been suggested that the response to replacement therapy with thyroxine and the thyrotropic hormone would measure the inherited capacity or deficiency of the pituitary and thyroid glands for the production of optimum amounts of thyroxine.

Upon such an interpretation of the observations it might be expected that individual cows would vary greatly in their response to thyroxine and further that the response would vary with the stage of lactation, environmental temperature, and possibly other factors.

In view of the possibility that such studies would help to explain one phase of the physiologic mechanisms involved in the inheritance of milk secretion, some preliminary observations which are believed to be of general interest were made during the past year.

### PLAN OF EXPERIMENT

The hormone of the thyroid gland is unique in that the oral administration of desiccated thyroid tissue in man is usually considered as efficient a mode of administration as the injection of an equivalent amount of thyroxine (Thompson et al., 1934). Since feeding is a more convenient method of administration, it seemed desirable to determine whether or not the two methods are also equally efficient with ruminants.

The experiment was divided into two phases, (a) the feeding of desiccated thyroid at levels of 1 to 2 ounces daily, and (b) the

daily injection of 5 to 10 mg. of thyroxine. Cows in varying stages of lactation were used (Tables 1 and 2).

The cows were weighed on three consecutive days each week in order to determine average body weight. The cows were fed all of the roughage they would clean up and grain was fed according to milk production. The cows were kept in a dry lot throughout the experiment, and were milked twice a day. Two-day composite samples were obtained weekly for fat and specific gravity determinations. The percentage of fat was obtained by the Babcock method; specific gravity by means of the Westphal balance; and the total solids and solids-not-fat computed according to the method of Sharp and Hart (1936). In our laboratory this technique has been found to give a specific gravity lower than that obtained at the usual temperature of 60°F., but the total solids agree closely with the drying method.

Pulse rates were obtained night and morning just before milking. The pulse was counted by feeling the posterior tibial artery on the medial surface of the tibia at a point eight to ten inches above the hock joint.

The desiccated thyroid fed was U. S. P. Grade guaranteed to contain not less than 0.2 per cent iodine. The thyroxine used was obtained from Hoffmann-La Roche, Nutley, New Jersey, and the British Drug Houses, London. The thyroxine was dissolved in water by means of sodium hydroxide.

TABLE 1.—DESCRIPTION OF COWS FED DESICCATED THYROID GLAND.

Herd No.	Breed	Age (yrs.)	Lactation	Weeks in Milk	Average Daily Milk (lbs.)	Body Weight (lbs.)
632	Holstein	9.0	(peak of production)	6	59	1430
428	Guernsey	7.5	(declining phase of lactation)	5	14	870
853	Jersey	4.5		3	25	825
665	Holstein	5.0		3	40	1215
717	Holstein	2.0		1	27	1140
874	Jersey	2.0	(declining rapidly)	1	14	870

TABLE 2.—DESCRIPTION OF COWS INJECTED WITH THYROXINE.

Herd No.	Breed	Age (yrs.)	Lactation	Weeks in Milk	Average Daily Milk (lbs.)	Body Weight (lbs.)
437	Guernsey	3	(peak of production)	2	38.8	1010
432	Guernsey	3		2	24.6	1075
713	Holstein	2	(declining phase of lactation)	1	40.0	1094
715	Holstein	2		1	29.0	1195
716	Holstein	2		1	33.0	1011
867	Jersey	3		1	28.0	892
607	Holstein	6		4	39.9	1206

## RESULTS OF THE EXPERIMENT

### 1. Feeding Thyroid

(a) **At the Peak of Production.**—A Holstein cow, No. 632, was fed desiccated thyroid at the rate of 1 ounce daily, starting the sixth week of lactation when she was producing at her maximum (58 pounds daily). This cow weighed about 1430 pounds at the start of the experiments and was in a good state of flesh. The feeding of thyroid substance was continued for eight weeks.

For the four weeks following the initiation of thyroid feeding the milk production declined slightly, but remained at a surprisingly constant level, averaging 56 pounds daily. Body weight decreased slightly, averaging 1406 pounds, at the end of the second week, and 1402 pounds at the end of the fourth week.

The pulse rate was observed to increase an average of four beats per minute above the average 65 beats per minute obtained for the two week period prior to the feeding of the desiccated thyroid. At the end of the fourth week, however, the average pulse rate was approximately normal. Throughout the four week period the percentage of butterfat ranged from 3.5 to 3.8 per cent, the same as that observed prior to the feeding of thyroid.

Between the fourth and eighth week of the experiment the daily yield showed a gradual decline. The average production for the fifth week was 55 pounds of milk daily with an average fat content of 3.7 per cent, but by the eighth week had declined to 48 pounds with a test of 3.1 per cent butterfat. The solids-not-fat content of the milk appeared to be unaffected, but due to the decline in fat percentage the percentage of total solids was lowered materially averaging 10.81 per cent at the end as compared to 11.6 per cent at the beginning of the experiment. Body weight had declined to 1390 pounds and the pulse rate remained normal.

Thyroid feeding was then discontinued for four weeks, and the regular feeding of grain, hay and silage was continued at the usual level. Milk production declined fairly rapidly during this period, dropping from an average of 48.4 pounds daily to 42.7 pounds for the fourth week after thyroid feeding was discontinued. The pulse was slightly slower, averaging 58 to 60 beats per minute and body weight increased from 1390 to 1434 pounds.

After the four week rest period, a second phase of feeding desiccated thyroid was begun. Two ounces daily were fed as a part of the grain ration. This rate of feeding was continued for five weeks, during which time the milk yield declined from 42 to 39 pounds

daily. In an attempt to stimulate greater production the daily dose of thyroid substance was increased to four ounces. This practice was reflected by a sharp decline in milk production. At the end of the first week the daily average was only 35.9 pounds as compared to 39 pounds at the beginning. Resumption of the plan of feeding 2 ounces daily resulted in an average increase of 2 pounds daily for the succeeding week. After three weeks of feeding thyroid at this level the daily milk yield averaged 35 pounds. At the end of the 20th week on experiment, thyroid feeding was discontinued and milk production dropped from 35 to 31 pounds daily.

These data indicate that thyroxine was probably not a limiting factor in production of this cow during the period of maximum yield. During the feeding of two ounces of desiccated thyroid in the declining phase of lactation there was a slight diminution in milk yield. There is, however, some indication that the fat yield and the persistency of lactation were benefited, for upon the discontinuation of feeding thyroid, milk production dropped off rapidly. Possibly one ounce daily would have been adequate during the declining phase.

(b) **During Declining Production.**—When a group of four cows averaging 28 pounds of milk daily and varying from the 9th to the 22nd week of lactation (Table 1) were fed 1 ounce of thyroid daily, the pulse rate increased slightly (7 to 8 beats per minute above the normal of about 60). The increase in production was

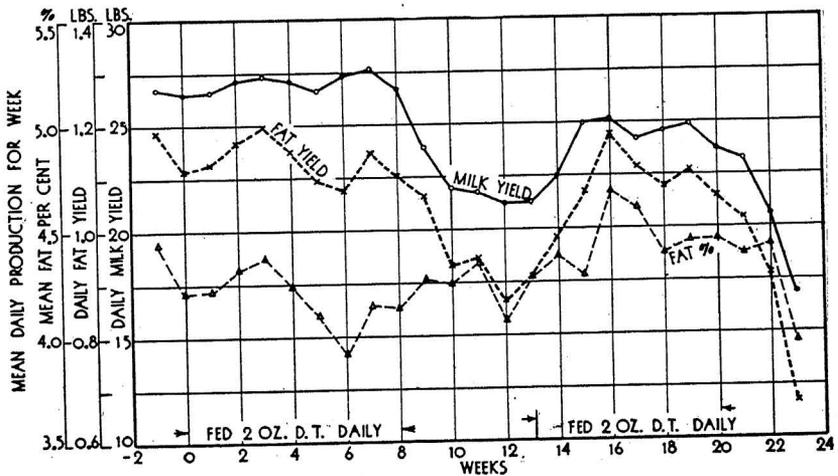


Fig. 1.—Effects of Feeding Desiccated Thyroid to Cows Starting Decline in Production.

insignificant, although a slight increase in fat yield occurred (Table 3). At the end of four weeks the amount of thyroid fed was increased to 2 ounces daily per cow. Production was maintained at about the same level until the end of eight weeks, when feeding was discontinued. A precipitous drop in milk secretion during the next two weeks (Fig. 1 and Table 3), would appear to indicate that maintenance of the previous high level was due to the feeding of thyroid. This is further substantiated by the fact that at the end of a four week rest period resumption of thyroid feeding resulted after four weeks in an average increase in milk yield of 18.2 per cent and in fat yield of 35 per cent. The average daily milk production increased about four pounds and the average daily fat yield increased from 0.86 to 1.178 pounds at the end of the 16th week (Table 3).

TABLE 3.—PRODUCTION OF COWS FED DESICCATED THYROID.  
(Average daily production of Cows 428, 853, 665, 717)

Month	Week on experiment	Daily Milk Yield (lbs.)	Fat %	Daily Fat Yield (lbs.)	Solids-not-fat %	Desic. Thyroid fed daily ozs.	Increase in milk yield %	Increase in fat yield %
Dec.	1	26.71	4.44	1.186	8.51			
	2	26.45	4.21	1.116	7.96			
Jan.	1	26.61	4.22	1.125	8.58	1		
	2	27.12	4.31	1.168	9.15	1		
	3	27.34	4.37	1.197	8.50	1		7.20
	4	27.21	4.24	1.154	8.25	1		
	5	26.69	4.10	1.096	8.64	2		
Feb.	6	27.33	3.92	1.073	8.72	2		
	7	27.60	4.15	1.147	8.43	2	4.3	
	8	26.61	4.13	1.100	8.35	2		
Mar.	9	24.90	4.26	1.063	8.21			
	10	21.98	4.24	0.923	8.39			
	11	21.75	4.35	0.945	7.79			
	12	21.26	4.07	0.865	8.10			
Apr.	13	21.28	4.29	0.913	8.13	2		
	14	22.48	4.38	0.985	8.24	2		
	15	24.97	4.28	1.068	8.19	2		
	16	25.14	4.68	1.178	8.27	2	18.2	35.0
	17	24.21	4.60	1.115	8.57	2		
	18	24.57	4.39	1.080	8.55	2		
	19	24.93	4.45	1.110	8.72	2		
May	20	23.77	4.45	1.058	8.65	2		
	21	23.21	4.38	1.019	8.31			
	22	20.68	4.43	0.916	8.37			
	23	16.93	3.96	0.670	8.64			

An increase in total milk, fat percentage, and absolute fat thus resulted. The cessation of thyroid feeding at the end of the 20th week was followed by an immediate decrease in both milk yield and fat percentage. The average decrease in daily milk yield was approximately 33 per cent, with the average daily fat yield lowered 43 per cent.

The individual cows used on this phase of the experiment showed decidedly varying responses to the feeding of desiccated thyroid, even though most of them were in similar stages of lactation. Cow No. 428, started on the experiment during the fourteenth week of lactation and when she was producing an average of 14 pounds of milk daily, showed little response to the first eight weeks of thyroid feeding although her daily milk and fat yield remained nearly constant. At the termination of thyroid feeding, however, the yield of milk dropped from 13.6 to 10.7 pounds. After a four week rest period, the feeding of desiccated thyroid was resumed and continued for an additional eight weeks. By the end of the seventh week the milk yield had reached a level of 12.73 pounds daily, an increase of 18 per cent, with the daily fat yield raised 11 per cent above the non-thyroid feeding period. Thus in the 32nd week of lactation the daily milk and fat yields were comparable to that of the fourteenth or beginning week of the experiment.

Cow No. 853 also received desiccated thyroid starting with the fourteenth week of lactation. She was then producing approximately 22 pounds of milk daily. After receiving 1 to 2 ounces of thyroid substance daily for eight weeks the daily milk yield averaged 19.8 pounds, with the fat yield and percentage of fat showing little change. Thyroid feeding was discontinued for four weeks, during which time the milk yield decreased from 19.8 to 13.6 pounds daily, the percentage of fat, however, increased from 5.2 to 6.4. Thyroid feeding was resumed and continued for eight weeks. The milk production increased from 14 pounds to 16.5 pounds daily, or approximately 20 per cent, with a slight increase in test and total fat yield.

The greatest individual response of cows in the group was obtained with cow No. 665, a Holstein, producing 40 pounds of milk daily in the 22nd week of lactation when she was placed on the experiment. For eight weeks, during which time 1 to 2 ounces of desiccated thyroid were fed daily, she averaged from 32 to 45 pounds of milk per day (a 12 per cent increase) with an increase also in fat percentage. The discontinuance of the thyroid substance in the ration for four weeks resulted in a decrease of milk yield of 12 pounds daily by the end of the third week. The average daily production for that week, the thirty-third week of lactation, was 32.08 pounds. The next week, however, production increased to 36 pounds daily. When the feeding of desiccated thyroid was resumed for an eight week period, however, milk and fat yield rose considerably averaging 43.2 pounds of milk with a 4.1 per cent

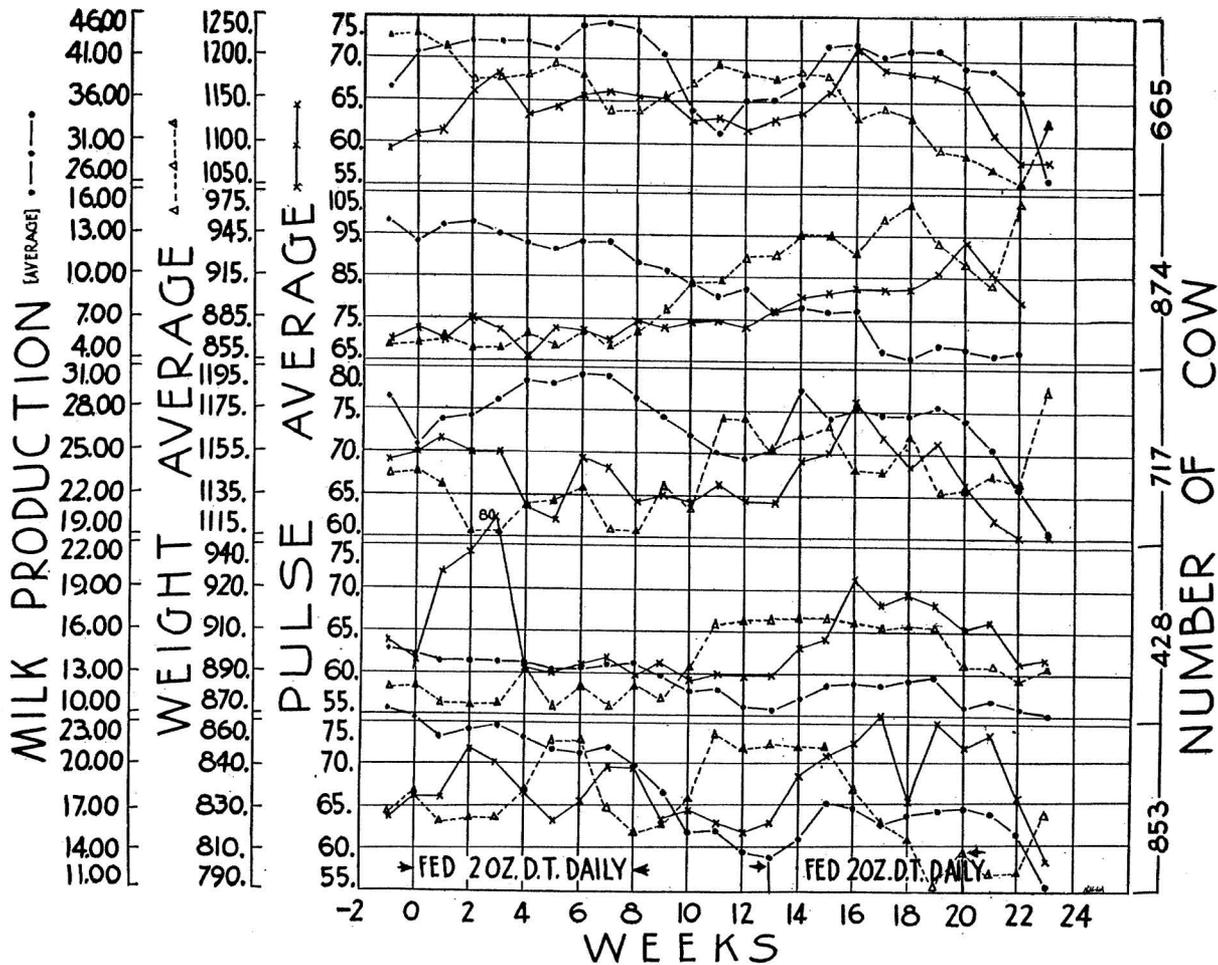


Fig. 2.—Effects of Thyroid Feeding on Milk Production, Body Weight, and Pulse Rate.

test for the fourth week. This increase amounts to 35 per cent for the milk yield and nearly 54 per cent in total fat yield.

Cow No. 717, also a Holstein, started on experiment 9.5 weeks after freshening when producing 27 pounds of milk daily showed a gradual increase during the first eight week feeding period. Starting with the second week, the daily milk yield rose an average of about one pound daily each week, and at the end of the sixth week she was producing 30.3 pounds daily, an increase of about 10 per cent. The fat yield increased 16 per cent during the period, with the percentage of fat rising from 3.0 at the starting point to 3.5 at the end of the eighth week. During the four week rest period the same type of decline as described for the other members of the group was experienced. The daily milk yield dropped from an average of 29 pounds to about 24 pounds. The second eight weeks of feeding desiccated thyroid, however, resulted in an increase in milk yield of about 16 per cent. Seven weeks after the second phase of feeding was begun, the milk yield had increased to 28 pounds daily, one pound per day more than the starting level 19 weeks previous.

**(c) During a Rapid Decline in Production.**—A Jersey cow (No. 874) 21 weeks in lactation, producing an average of 14 pounds daily, but decreasing rapidly in milk yield, was fed two ounces of thyroid substance daily. At the end of the 8th week of thyroid feeding the cow averaged 11 pounds of milk daily. Cessation of thyroid feeding for four weeks resulted in a decrease to 9 pounds of milk daily. Resumption of thyroid feeding (2 ounces daily) at this point resulted in a rapid decline and at the end of four weeks the cow yielded only 4.8 pounds of milk daily. Thyroxine injection at the rate of 10 mg. daily for two weeks was then tried, but the level of milk secretion was not influenced. The pulse rate rose rapidly during this time, attaining a level of 95 beats per minute. Body weight decreased very markedly (Fig. 2). This would indicate that even though the general metabolic level is raised, some cows nearing the end of lactation cannot be increased in milk and fat yield by the use of thyroxine.

#### **Pulse Rate, Body Weight, and Feed Consumption.**

Thyroxine, the active constituent of the thyroid gland, as previously pointed out, affects tremendously the metabolic rate when available in sufficient quantity. It is of interest, therefore, to note in every instance that the feeding of desiccated thyroid resulted

in an increase of the pulse rate (Fig. 2). In some instances the increase amounted to only five to eight beats per minute. In other cases such as in cow No. 853, the increase was somewhat greater. It will be noted that an increase in pulse rate is associated with a rise in milk yield and a decrease in body weight. Although in the first eight weeks of the experiment no marked increase was observed, it is significant, that during the ninth to the twelfth weeks inclusive, when no thyroid substance was fed, that there followed a slowing of the pulse rate, a diminution in milk yield, and a rapid gain in body weight (Fig. 2). This trend is fairly striking for all cows concerned. The cows were fed their regular hay, silage, and grain at the usual levels, but in the absence of the stimulating effect of thyroxine, it is evident that the demand of the mammary gland is considerably below that of the thyroid feeding period. During the second feeding period (13th-20th week), the feeding of two ounces of desiccated thyroid resulted in a rapid increase in the pulse rate amounting to 10 to 15 beats per minute on the average (Fig. 2). As has been pointed out, the greatest increase in milk and fat yield, due to the feeding of thyroid substance, was obtained during this phase of the experiment. Associated with the average increase of 18 per cent in milk yield and 36 per cent in fat production is a very rapid loss in weight. The cows showing the greatest response by an increase in milk and fat yield suffered the largest weight losses. Cow No. 665 for instance, increased her milk yield to the extent of 35 per cent above the base level after receiving two ounces of desiccated thyroid for four weeks. Her weight declined from 1188 to 1136 pounds, and after eight weeks of feeding at this level she weighed only 1080 pounds, a body loss of over 100 pounds.

Cow No. 874, treated during the declining phases of lactation, failed to respond with an increase in production, but in spite of a decline in milk yield there was a marked rise in the pulse rate and a decrease in body weight (Fig. 2).

In general the increase in pulse rate was proportional to the amount of thyroid substance fed. Two ounces daily resulted in a greater increase than one ounce. The fact that the cows were more advanced in lactation at the time two ounces per day were fed, may be a factor influencing the effectiveness of the thyroid substance inasmuch as the experiments of Graham (1934) indicate that cows show much greater response to thyroxine during advanced lactation.

## II. Injection of Thyroxine.

(a) **At the Peak of Milk Production.**—Two cows (432G and 437G) at the peak of production were selected for this experiment. In their first lactation they had averaged 311 and 264 pounds of butterfat, respectively, under Advanced Registry conditions. If their relatively low productive ability was due to a thyroid deficiency it might be expected that they would show an increase in milk yield at this time. However, the injection of 10 mg. of thyroxine daily for two weeks caused in both a depression of milk secretion. It seems clear that in these two cows the limiting factor in the low inherited production was not a lack of thyroxine secretion at the time of maximum production (Table 4). Both cows showed an increase in pulse rate of 15 to 20 beats per minute and lost weight to the extent of 50 to 70 pounds each in a two week period (Fig. 3). Cow 432G dropped from a daily level of 24.8 pounds to 22.2 pounds of milk following thyroxine injection, and No. 437G decreased from a starting level of 39.7 pounds to 34.8 pounds. Both cows decreased rapidly in yield after thyroxine administration was discontinued.

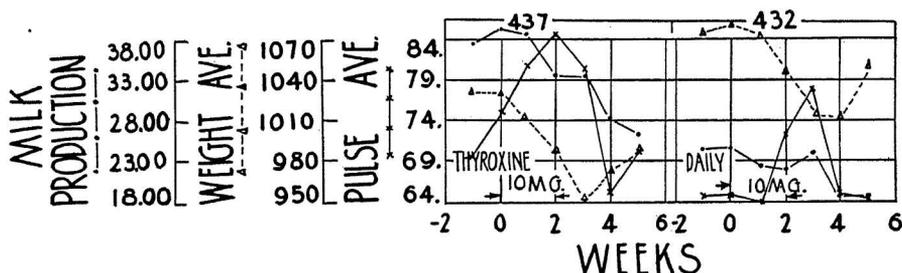


Fig. 3.—Effects of Thyroxine Injection on Milk Production, Body Weight, and Pulse Rate.

These results bear out the observation of Graham that thyroxine injection at the peak of production may cause a diminution in the yield of milk and fat (Fig. 3).

(b) **During the Decline in Production.**—A group of four cows was first injected with 5 mg. daily of thyroxine for three weeks. These cows showed an average increase in milk secretion of 11 per cent and of 22 per cent in fat yield (Table 5). The cessation of thyroxine injection resulted in a rapid decline in milk yield. The fat percentage, however, reached its peak the first week after the omission of thyroxine.

Resumption of thyroxine injection at 10 mg. levels daily for 15 days when the cows were in the 27th week of lactation again showed the striking effect of thyroxine on milk and fat secretion of cows in declining lactation. At the end of the 15 day injection period the cows were producing an average of 22 per cent more milk and 37 per cent more fat, based on weekly averages for the group, than at the start of the second injection period. The cessation of thyroxine injection again resulted in a rapid decline in milk production. Fourteen days after the last injection the cows were averaging 7.1 pounds per day, or about 30 per cent less milk than during the injection period (Fig. 4).

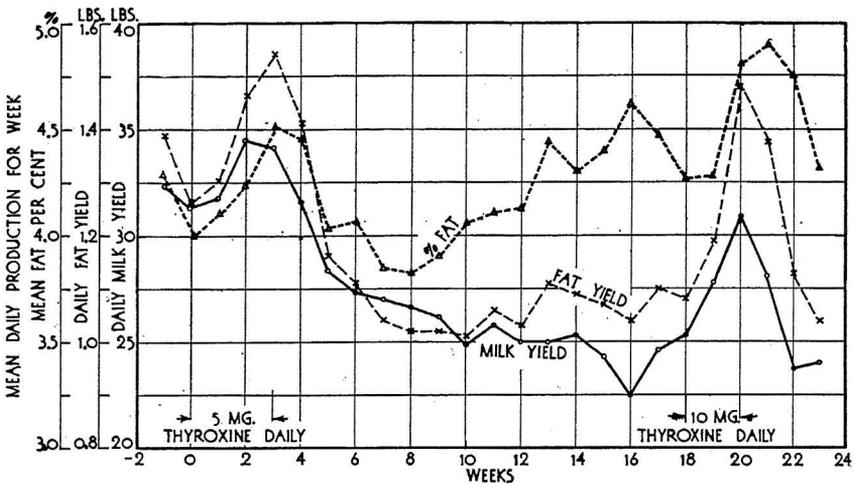


Fig. 4.—Effects of Thyroxine Injection on Cows Starting Decline in Production.

In this same series of experiments, Holstein cow No. 607 (see Table 4 and Fig. 5) was injected beginning the 16th week of lactation, with 10 mg. of thyroxine daily for 15 days. The same results as obtained for other cows in declining lactation were experienced, an increase of 12 per cent milk yield and 18 per cent in total fat production was observed.

In this series of experiments, as was observed in the feeding of desiccated thyroid, there was considerable difference in the response of individual cows. Cow No. 713 responded with an increase in daily milk yield of about 3 pounds, or 11 per cent during the first series of thyroid injections which were at the rate of 5 mg. daily. After a lapse of 15 weeks the production of milk was in-

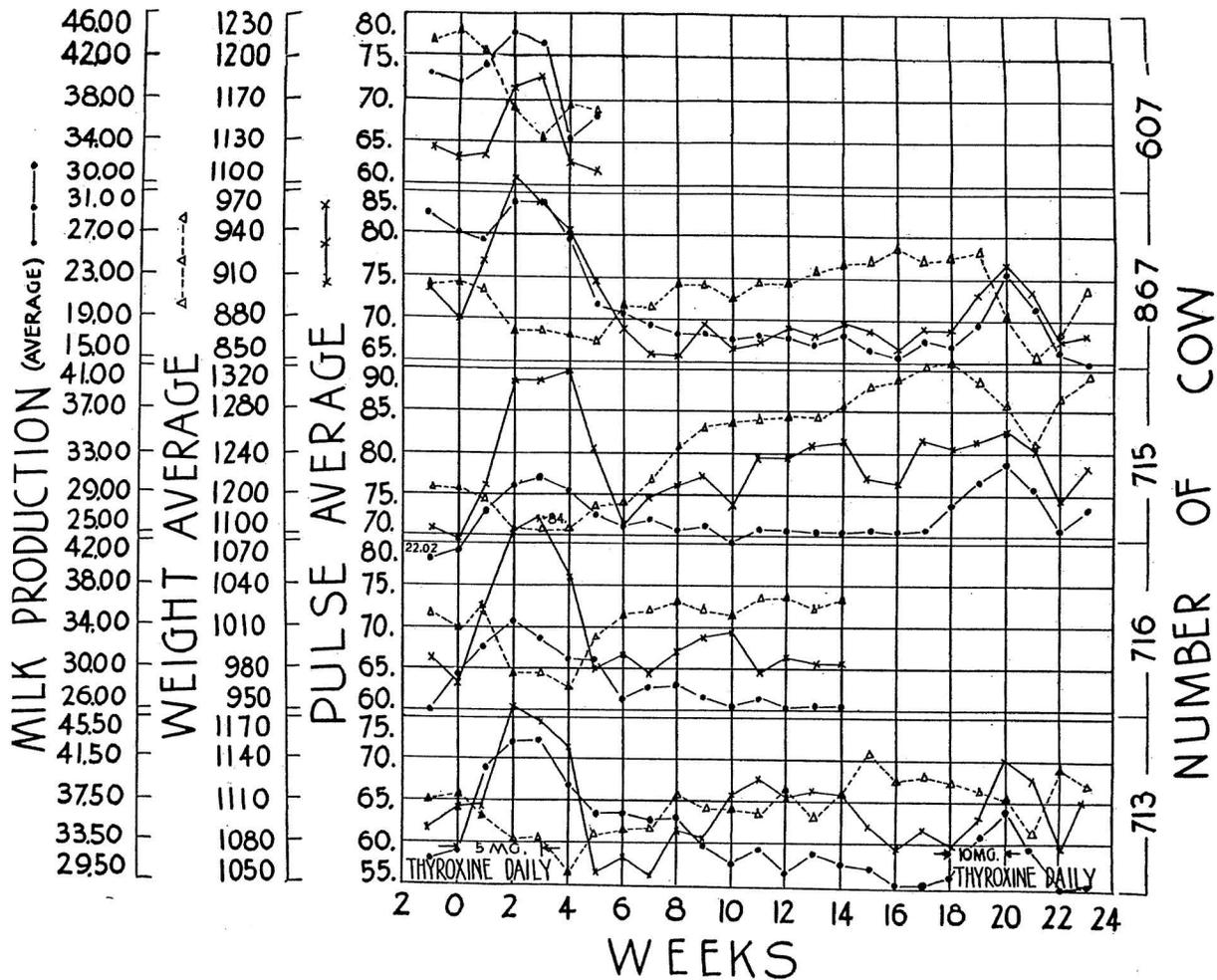


Fig. 5.—Effects of Thyroxine Injection on Milk Production, Body Weight, and Pulse Rate.

TABLE 4.—EFFECTS OF THYROXINE INJECTION (INDIVIDUAL RECORDS).

Herd No. and Breed	Weeks on Experiment	Weeks in Milk	Daily Milk (lbs.)	Fat %	Daily Total Fat (lbs.)	Solids-not-fat* %	Daily Thyroxine Treatment	
437G	1		(Cows at peak of production)					
				37.95	5.1	1.94	8.70	
	2		39.70	4.7	1.87	8.40		
	1		3	38.54	4.7	1.81	8.42	10 mg.
	2		34.79	5.3	1.84	9.40	10 mg.	
437G	3		38.68	5.6	1.89	9.17		
	4		28.27	5.5	1.54	8.91		
	5		26.20	4.4	1.15	9.00		
	1		24.24	4.3	1.05	8.71		
	2		24.08	4.5	1.12	8.63		
437G	1	7	22.68	4.2	0.95	8.72	10 mg.	
			22.24	4.5	1.00	8.79	10 mg.	
	3		24.32	5.4	1.31	8.49		
	4		18.44	5.5	1.01	8.57		
	5		18.52	5.0	0.93	8.77		
607H	1		(Cow in declining lactation)					
				40.27	3.7	1.49	8.40	
	2		39.14	3.5	1.37	8.37		
	1		16	41.68	3.5	1.46	8.44	10 mg.
	2		44.74		1.74	8.37	10 mg.	
607H	3		43.25	4.2	1.32	8.31		
	4		34.20	4.1	1.40	8.21		
	5		37.90	3.3	1.25	7.99		

\*Calculated specific gravity determined according to Sharp and Hart (1936).

TABLE 5.—PRODUCTION OF COWS INJECTED WITH THYROXINE.  
(Average daily production of Cows 713, 715, 716, 867)

Month	Week on experiment	Daily Milk (lbs.)	Fat %	Daily Total Fat (lbs.)	Solids-not-fat %	Thyroxine Treatment daily	Increase in milk yield %	Increase in fat yield %
Dec.	1	32.4	4.29	1.39	8.359			
	2	31.3	4.00	1.26	8.270			
Jan.	1	31.8	4.09	1.30	8.340	5 mg.		
	2	34.5	4.23	1.46	8.524	5 mg.	11.1	22.2
	3	34.2	4.51	1.54	8.523	5 mg.		
Jan.	4	31.6	4.46	1.41	8.405			
	5	28.8	4.02	1.16	8.034			
	6	27.3	4.06	1.11	8.686			
Feb.	7	27.0	3.85	1.04	8.458			
	8	26.7	3.82	1.02	7.764			
	9	26.1	3.91	1.02	8.207			
March	10	24.9	4.06	1.01	8.250			
	11	25.8	4.10	1.06	7.754			
	12	25.0	4.12	1.03	8.071			
	13	25.0	4.44	1.11	8.200			
Apr.	14	25.3	4.31	1.09	8.116			
	15	24.3	4.40	1.07	8.357			
	16	22.5	4.63	1.04	8.348			
	17	24.6	4.47	1.10	8.449			
	18	25.3	4.27	1.08	8.450			
Apr.	19	27.8	4.28	1.19	8.770	10 mg.	23.0	37.0
May	20	30.9	4.80	1.48	8.678	10 mg.		
May	21	28.1	4.91	1.38	8.297			
	22	23.8	4.75	1.13	8.278			
	23	24.1	4.32	1.04	8.689			

creased 15 per cent by the injection of 10 mg. of thyroxine daily. The total fat content seemed most affected and increased 35 per cent in both instances.

No. 715 responded with an increase in milk yield of about 18 per cent on the first series of injections, while the total fat yield increased 12 per cent. On the second series of injections her daily milk production increased 32 per cent, an actual rise of over 5 pounds daily, and an increase in fat percentage with the result that the total fat yield was raised 65 per cent above the lowest, non-injection level.

Cow No. 716 was continued on the experiment only during the first injection period, but responded with an increase in milk amounting to about 10 per cent with the total fat yield increased 8 per cent.

Cow No. 867, a Jersey, started on the experiment the eighth week of lactation when producing at a level of 27 pounds of milk daily, gave a decided response to the first series of thyroxine injections. The milk production increased 3 pounds or 14 per cent, and the total fat production about 28 per cent above the base period. After a lapse of 15 weeks the injection of thyroxine was resumed with the result that the average daily milk yield rose from 16 to 23 pounds and the total weekly butterfat yield increased nearly 4 pounds during the second week of injections. These increases in milk and fat amount to 44 and 56 per cent, respectively.

#### **Body Weight, Pulse, and Feed Consumption.**

The data showing changes in pulse rate, body weight, and milk yield during thyroxine administration are plotted in Fig. 5. The cows undergoing treatment were found to lose weight to the extent of 4 to 6 per cent, but rapidly regained this weight and often showed a slight increase when administration was discontinued (Fig. 5). These facts, coupled with an increase of approximately 10 to 20 beats of the heart per minute, would seem to indicate that during thyroxine or desiccated thyroid administration the cows showing an increase in production were using materials obtained from their body tissues for the purpose of milk secretion.

The cows were fed according to the Morrison Standard and in view of the slight loss in body weight during injection or feeding of thyroxine this level of food intake was deemed sufficient.

### Solids-not-fat.

The effect of thyroid feeding and thyroxine injection on the solids-not-fat content of the milk produced by cows undergoing treatment in these experiments seems to be somewhat variable. In general a slight increase in solids-not-fat seems apparent during administration of the desiccated thyroid or thyroxine. However, the variations from week to week render it a little difficult to draw conclusions. In every case, however, (Tables 3, 4 and 5) the solids-not-fat increased slightly, both in total yield and percentage. Jack and Bechdel (1935) found the composition of milk little affected by thyroxine injection, but Folley and White (1936) reported increases both total and percentage of solids-not-fat. Our results would seem to agree with those of Folley and White, but are not as marked as the increases they report.

### The Comparative Response Obtained by the Injection of Thyroxine and the Feeding of Desiccated Thyroid.

The relative efficiency of thyroxine, administered by injection, and desiccated thyroid administered orally, in stimulating milk and butterfat yield, is of considerable interest. It has been pointed out that there was considerable difference in the effect on individual cows by the administration of thyroxine either by injection or by the feeding of the desiccated thyroid gland. The group of cows which were fed desiccated thyroid, (Tables 1 and 3), it will be noted, showed a 4 per cent, or insignificant increase in milk and butterfat yield when fed from 1 to 2 ounces of the thyroid substance daily during the early stages of lactation. The period of lactation for cows in this group ranged from 9½ to 22 weeks, with an average of 12 weeks. The average daily milk yield at the start of the first feeding period was 26 pounds. The second period of feeding, some 13 weeks later, and the 25th week of lactation on the average resulted in an increase in milk of 18 per cent, while the fat yield was increased 35 per cent. In the second phase of feeding, 2 ounces of desiccated thyroid were fed daily for a period of eight weeks. In the first feeding experiment, it was observed that 1 ounce of desiccated thyroid failed to give a significant increase in pulse rate.

The cows injected with thyroxine (Tables 2 and 5) had been in milk from 7 to 16 weeks, or an average of 10 weeks, and were producing an average of 34 pounds of milk daily. Five mg. of thyroxine injected daily for three weeks gave an average increase of 11 per cent in milk and 22 per cent in butterfat yield above the

base period. When injections were resumed after an interval of about 15 weeks, 10 mg. of thyroxine were injected daily for two weeks. The milk yield rose 23 per cent, and the total daily fat yield, based on weekly periods, rose 37 per cent above the average of the last week of the non-injection period.

Thus it was observed that in a general way the response in increased milk and butterfat yield obtained by the amounts of thyroxine injected was considerably greater than by the feeding of desiccated thyroid. Particularly is this true in the first part of the experiment when 1 to 2 ounces of desiccated thyroid fed daily scarcely changed the milk yield and butterfat yield increased only 7 per cent, but 5 mg. of thyroxine injected daily raised the milk yield 11 per cent and the butterfat yield 22 per cent. The metabolic changes thus effected were markedly in favor of the thyroxine. The relative changes in yield produced by the feeding of 2 ounces of desiccated thyroid daily as compared to 10 mg. of thyroxine injected daily are fairly comparable during the second phase of the experiment (Tables 3 and 5).

Thyroxine contains, on the average, 65 per cent iodine. The desiccated thyroid used was guaranteed to contain not less than 0.2 per cent iodine. On this basis the relative amount of thyroxine administered by the feeding of desiccated thyroid may be estimated. Two ounces (56.7 grams) of desiccated thyroid daily would supply 113.4 mg. of iodine. If we assume all of the iodine present to exist as a constituent part of the thyroxine molecule, which may however be questionable because the thyroid gland is recognized as storing tremendous amounts of iodine, it would appear that some 153 mg. of thyroxine were administered daily. This is approximately fifteen times more than was necessary, when administered by subcutaneous injection, to produce a comparable increase in milk and butterfat yield. The cause for this difference in effectiveness is not entirely clear, but the observations of Thompson et al. (1935) in studying the calorogenic activity of desiccated thyroid throws some light on the situation. In clinical use, these investigators found that a single dose of a certain lot of desiccated thyroid was only 52 per cent as effective as thyroxine injected intravenously in maintaining the desired metabolic level and the ratio of the difference in effect of the two substances varied greatly from patient to patient. These findings were not in keeping with the reports of Hunt and Seidell (1908), Means, Lerman and Salter (1933) and Thompson et al. (1933) which indicated that the calorogenic activity of desiccated thyroid was proportional to its iodine

content. Harrington and Randall (1929-1931), however, isolated diiodotyrosine from the thyroid by alkaline hydrolysis and by the use of proteolytic enzymes and concluded that at least 50 per cent of the total iodine of the thyroid gland was present in this form. Diiodotyrosine has very little calorogenic effect and experiments by Thompson et al. (1934a) indicate it may be only about one ten-thousandth as effective as thyroxine in changing the metabolic level. Further experiments (Thompson et al., 1935) show that most of the calorogenic properties of desiccated thyroid are contained in the acid insoluble portion, obtained by digesting the substance with pepsin. They further indicate that this fraction contains only about 45 per cent of the total iodine of the desiccated thyroid, but is more effective, per milligram of iodine, in metabolic response than the original substance from which it was prepared. These observations point out the danger of comparing the effectiveness of thyroxine and desiccated thyroid on the basis of its iodine content.

A matter of still further concern in explaining the lower efficiency of desiccated thyroid, orally administered to cattle, in promoting an increase in milk and butterfat yield, is the finding by Cameron and Carmichael (1926) and Thompson et al. (1934b) that the heating of desiccated thyroid substance in alkaline solution reduces its calorogenic activity about two-thirds. Thyroxine heated in the same manner is not altered in calorogenic effect. In man, orally administered desiccated thyroid passes directly into the stomach where an acid-pepsin media exists. In the rumen, however, the thyroid substance fed along with the food passes into the rumen, reticulum, and omasum before it reaches the true stomach or abomasum. The rumen and reticulum are alkaline in reaction. No true digestion takes place in any but the true stomach which usually contains a little less than 0.5 per cent acid. There is, however, considerable bacterial action on the foodstuffs in the rumen. These conditions, it would appear, favor a mild alkaline hydrolysis of the desiccated thyroid substance. While the temperature within the rumen is not great, it is entirely possible that the calorogenic activity of the thyroid material might be altered to a considerable extent. It is believed this may explain in part the wide difference between the human and the bovine in the efficient utilization of desiccated thyroid.

## DISCUSSION

How thyroxine stimulates milk secretion is an open question. It has been suggested that it is due to the stimulation of greater general body metabolism involving also the cells of the mammary gland (Graham, 1934). It is well known that with a more rapid heart beat more blood will be available to all parts of the body. It would be expected that more blood would flow through the udder. However, with increased general metabolism the tissues would compete with the udder for the precursors of milk in the blood. If this competition were excessive a reduction in milk secretion would result.

Graham et al. (1937) observed in the case of three cows that during a period of thyroxine injection the uptake of both sugar and fatty acids from the blood by the udder was increased. This observation is the more remarkable due to the fact that while the arterial sugar increased the fatty acids were lowered.

Jack and Bechdel (1935) suggested the theory that the favorable influence of thyroxine on milk secretion was an indirect effect by way of the pituitary. The hyperthyroid condition was thought to stimulate an increased secretion of the lactogenic hormone. It is true that thyroid feeding in rats increased the amount of gonadotropic hormone (Evans and Simpson, 1930; and Van Horn, 1933), but Reece and Turner (1937) observed a reduction of the lactogenic hormone in the male rat pituitary following thyroxine injection. Further work with lactating animals is required.

These data indicate that cows at the peak of production show little tendency to be stimulated to increased production by thyroxine, whereas after the decline sets in it is possible to increase or maintain milk secretion. It is possible that the rise and decline of the lactation curve represents a rise and decline in the secretion of all pituitary hormones which directly or indirectly influence the lactation process. If the production of the thyrotropic hormone by the animal increased for the first month or more, thus producing a hyperthyroid condition, the injection of additional amounts of thyroxine would result in a depression of milk secretion due to the competition of the hyperactive body tissues for the precursors of milk. Only animals whose pituitaries failed to function normally in this regard would be expected to increase in milk secretion during the period of maximum production.

Cows lacking persistency of milk secretion due to a decreased rate of secretion of the thyrotropic hormone (and probably other

pituitary hormones) would respond to the injection of thyroxine in proportion to the decrease in the rate of secretion of the hormone. If this were true it would be expected that cows most lacking in persistency would show the greatest response.

### SUMMARY AND CONCLUSIONS

A study was made of the effects of thyroxine, subcutaneously injected, and desiccated thyroid, orally administered, on the milk and butterfat yield of cows in various stages of lactation.

Desiccated thyroid, fed to a group of cows in declining lactation, at the rate of two ounces daily throughout an eight weeks period, was observed to bring about an average increase in milk yield of 18.2 per cent. The butterfat yield for the same period was raised 35 per cent above the base level. Cows at the peak of production, and those nearing the end of the lactation period, failed to increase in milk yield when desiccated thyroid was fed. There was, however, a slight increase in fat yield, probably as a result of metabolic disturbances.

The injection of thyroxine, in alkaline solution, at the rate of 5 mg. daily for three weeks was observed to bring about an increase of 11 per cent in milk and 22 per cent in butterfat yield where the cows were in the declining phase of lactation. Increasing the daily dosage of cows in the last half of lactation to 10 mg. of thyroxine for two weeks resulted in an average increase of 23 per cent in milk production and 37 per cent in butterfat yield.

The injection of thyroxine to cows at the peak of production, three to seven weeks after freshening, resulted in a diminution of both milk and fat yield. The hyperthyroidism brought about by the addition of thyroxine at this time resulted in a marked increase in pulse and respiratory rate and a rapid loss in weight, with deleterious effects on milk secretion. A cow practically dry was also found to respond adversely to thyroxine injection by a marked decrease in milk and fat yield.

The period of lactation, as well as the individuality of the cow, seems to be an important factor in affecting the results of thyroid substance, or thyroxine, on milk secretion.

The administration of thyroxine, either in the feeding of desiccated thyroid, or by the injection of synthetic thyroxine, showed an increase in pulse rate and a slight loss of body weight. The changes in metabolic rate seemed to markedly affect milk and fat secretion. Fat secretion appeared to be influenced more than milk yield by the treatment.

The solids-not-fat content of the milk produced by cows undergoing both types of thyroxine administration was slightly increased. There was generally a lowering of the daily solids-not-fat output when treatment was discontinued.

Thyroxine, injected subcutaneously, is more effective, from the standpoint of dosage required, in bringing about an increase in metabolic level, and a consequent effect on milk and fat yield, than desiccated thyroid orally administered. Ten mg. of thyroxine were found to produce an effect equal to and in most cases greater than that brought about by two ounces of desiccated thyroid. It is believed that the lowered efficiency of desiccated thyroid might be explained by the possibility (a) that the thyroid substance is partially inactivated in the rumen, reticulum, and omasum before it reaches the abomasum of the bovine; (b) the activity of desiccated thyroid may not be proportional to its iodine content, but only to a fraction of the iodine which accounts for most of the calorogenic effect.

#### REFERENCES CITED

- Cameron, A. T., and Carmichael, J. 1926 *An attempt to evaluate thyroid preparations utilizing their effect on growth rate and production of organ hypertrophy in the young white rat.* Tr. Roy. Soc., Canada, vol. 20, sec. 5, p. 1.
- Evans, H. M., and Simpson, M. E. 1930 *Some effects on the hypophysis of hyper- and hypothyroidism.* Anat. Rec., vol. 45, p. 215.
- Folley, S. J., and White, P. 1936 *The effect of thyroxine on milk secretion and on the phosphatase of the blood and milk of the lactating cow.* Proc. Royal Soc., London, Series B, vol. 120, p. 346.
- Fuller, J. M. 1928 *Some physical and physiological activities of dairy cows.* New Hampshire Agr. Exp. Sta. Tech. Bul. 35.
- Graham, Jr., W. R. 1934a *The effect of thyroidectomy and thyroid feeding on the milk secretion and milk fat production of cows.* J. Nutrition, vol. 7, p. 407.
- Graham, Jr., W. R. 1934b *The action of thyroxine on the milk and milk fat production of cows.* Biochem. J., vol. 38, p. 1368.
- Graham, Jr., W. R., et al. 1937 *A method for obtaining arterial blood from the goat.* Mo. Agr. Exp. Sta. Res. Bul. 260.
- Grimmer, W. 1918 *Beitrage zur Kenntnis der Milch schilddrusenloser Ziegen.* Biochem. Ztschr., Bd. 88, S. 43.
- Grimmer, W., und Paul, O. 1930 *Zur Kenntnis der Milch schilddrusenloser Ziegen.* II. Milchwirtsch. Forsch., Bd. 10, S. 336.
- Grueter, F. 1931 *Experimentell-Hormonale Beeinflussung der Milchsekretion unter besonderer Berucksichtigung von Kuhen and Ziegen.* Proc. 2nd. Internat. Cong. Sex Research (1930), p. 443. Edinburgh. Oliver and Boyd.
- Harrington, C. R., and Randall, S. S. 1929 *Observations on the iodine containing compounds of the thyroid gland; isolation of d1-3:5 Diiodotyrosine.* Biochem. J., Vol. 23, p. 373.
- Harrington, C. R., and Randall, S. S. 1931 *Isolation of d1-3:5 Diiodotyrosine from the thyroid gland by the action of proteolytic enzymes.* Biochem. J., vol. 25, p. 1032.

- Hunt, Reid and Seidell, A. 1908 *Studies on thyroid; I. Relation of iodine to the physiological activity of thyroid preparations*. Bul. 47, Hyg. Lab. U. S. P. H. S. Govt. Printing Office, Washington, D. C.
- Jack, E. L., and Bechdel, S. I. 1935 *A study of the influence of thyroxine on milk secretion*. J. Dairy Sci., vol. 18, p. 195.
- Means, J. H., Lerman, J., and Salter, W. T. 1933 *The role of thyroxine iodine and total organic iodine in the calorogenic action of the whole thyroid gland*. J. Clin. Investigations, vol. 12, p. 683.
- Reece, R. P. and Turner, C. W. 1937 *The lactogenic and thyrotropic hormone content of the anterior lobe of the pituitary gland*. Mo. Agr. Exp. Sta. Res. Bul. 266.
- Sharp, Paul F., and Hart, Ray G. 1936 *The influence of the physical state of the fat on the calculation of solids from the specific gravity of milk*. J. Dairy Sci., vol. 19, p. 683.
- Thompson, W. O., McLellan, L. L., Thompson, P. K., and Dickie, L. F. N. 1933 *The rates of utilization of thyroxine and of desiccated thyroid in man: the relation between the iodine in desiccated thyroid and in thyroxine*. J. Clin. Investigations, vol. 12, p. 235.
- Thompson, W. P., Thompson, P. K., Taylor, S. G., Alper, J. M., and Dickie, L. F. N. 1934 *The effect of various compounds of thyroxine on the basal metabolism*. Endocrinology, vol. 18, p. 228.
- Thompson, W. O., Alper, J. M.; Thompson, P. K., and Dickie, L. F. N. 1934(a) *The effect of diiodotyrosine on the basal metabolism in myxedema*. J. Clin. Investigations, vol. 13, p. 29.
- Thompson, W. O., Thompson, P. K., Taylor, S. G. and Dichie, L. F. N. 1934(b) *Preliminary report*—J. Clin. Investigation, vol. 13, p. 690.
- Thompson, W. O., Thompson, P. K., Taylor, S. G., Nadler, S. B. and Dickie, L. F. N. 1935 *The Pharmacology of the Thyroid in Man*. J. Am. Med. Assn., vol. 104, p. 972.
- Van Horn, H. H. 1933 *The relation of the thyroid to the hypophysis and ovary*. Endocrinology, vol. 17, p. 152.