The Effect of Thyroxine on the Metabolism of Lactating Cows

1. GENERAL RESULTS AND NITROGEN METABOLISM

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That thyroxine causes an increase in milk secretion and in the yield of milk fat has been shown by Graham (1934 *a*, *b*), Jack & Bechdel (1935), Folley & White (1936), Herman, Graham & Turner (1938) and Smith & Dastur (1940). These observations did not at first arouse general interest because of the prohibitive cost of thyroxine. Later, however, Ludwig & von Mutzenbecher (1939) showed that thyroid-active material could be produced from casein by iodination, and this was confirmed by Harington & Pitt-Rivers (1939), who demonstrated that in the iodination thyroxine was formed from the tyrosine of the casein. A few years later the conditions of iodination were further defined by Turner & Reineke (1944) in such a way as to ensure reasonable yields of thyroxine.

Since these observations were made, the use of iodinated casein for increasing the milk yield of cows in commercial herds has been investigated, notably by Blaxter (1945, 1946). Blaxter's work leaves little doubt that, when cows are given iodinated protein in their feed under ordinary conditions of farm management, the extra milk and milk fat produced result not from an increase in the intake of food, but from raised catabolism. The animals lose condition, probably because the extra milk is formed, in part at least, from the proteins and fat of the animals' own tissues during a period when the metabolic rate of the animals is increased. As increased catabolism might have marked adverse effects on lactating cows, the work described in the present paper was designed to determine to what extent the stimulation of milk production by thyroxine is associated with loss of body tissue and with negative nitrogen balance, and whether increase of food intake can compensate for any raised catabolism which may occur. For all the experiments thyroxine was used rather than iodinated protein, because of the risk that the activity of iodinated casein given orally would vary greatly from sample to sample and be difficult to assess. This uncertainty does not exist if a known dose of thyroxine is given subcutaneously.

EXPERIMENTAL

General plan of the experiments and care of the animals. Three experiments were carried out, each involving three Ayrshire cows which, at the beginning of the experiments, were 10–20 weeks from parturition. The animals were kept in special stalls in a metabolism house (Morris & Wright, 1933) in which the urine and faeces excreted by the cows can be collected separately with only slight mutual contamination. Before an experiment began, the cows were given a period of 2 or 3 weeks to accustom themselves to the metabolism house management and to the diets used in the experiment. This was followed by three periods, each lasting for at least 4 weeks. In the first and third periods no thyroxine was given, but in the second period two of the cows were treated with the hormone, the third cow receiving no thyroxine in any of the periods. In this way it was hoped to compare the findings obtained for the thyroxine-treated cows during the second period of each experiment with the findings for the same cows before and after thyroxine treatment, and also with those for the control cow throughout the whole experiment. This was possible for the first two experiments, but during the third experiment the control cow became ill, too late to be replaced, and had to be discarded. All the animals were weighed at the beginning and end of each period. Every 2 days, samples of food, urine, faeces and milk were analyzed.

Diet. In the first experiment the rations allowed per gallon of milk were purposely kept slightly below the lowest level which would ever be likely to be fed in practice. This resulted in negative N balances during the thyroxine period. In the second and third experiments the rationing was made progressively more liberal in order to determine how far the tendency to negative N balance could be overcome by increased food intake.

In the first experiment the maintenance ration consisted of 14 lb. hay and 1 lb. bruised oats/cow/day, and the production ration of 3·13 lb. bruised oats and 0·91 lb. bean meal (*Vicia faba*) per gallon of milk. The amount of production ration fed per day in any week was adjusted according to the yield of milk in the preceding week. The same production ration was fed in the second experiment but at a slightly higher level. In the third experiment the rations contained cubes consisting of wheat feed 42·5 %, decorticated groundnut 27·5 %, oats 20 % and molasses 10 %. For the first few weeks of the first control period of this third experiment, the maintenance ration was 14 lb. hay/day, and for production a mixture was made up consisting of equal parts of bruised oats, bean meal and cubes, 4 lb. of the mixture being fed per gallon of milk. Later in this first control period, in order to ensure that the animals would be liberally fed just before and during the thyroxine treatment, the allowance of hay was raised to 16 lb. and the concentrate mixture was changed to oats (3 parts), bean meal (3 parts) and cubes (4 parts), and fed at the rate of 5 lb. per gallon of milk on the basis of the yield during the previous fortnight. This basis of rationing was continued for the remainder of the experiment.

In work of this type, where attempts are made to feed rations strictly according to milk yield, it is not easy to be certain that the intended relationship between milk production and protein intake will be accurately maintained, since quite unpredictable variations in milk yield tend to occur. The best way of ascertaining what the relationship actually was, is to calculate it at the end of the experiment from the figures obtained for the milk yield and for the actual amount of protein eaten. Data obtained in this way for the amount of protein fed per gallon of milk are shown in Table 1.

Table 1. *Protein equivalent ingested (lb./gallon of milk yielded)*

Exp. no.	Cow no.	Period 1 (no thyroxine)	Period 2 (thyroxine)	Period 3 (no thyroxine)
1	1	0·51	0·50	0·77
	2 (control)*	0·44	0·41	0·44
	3	0·52	0·39	0·65
2	4	0·58	0·57	1·00
	5 (control)*	0·53	0·56	0·55
	6	0·50	0·52	0·95
3	7	0·62	0·68	0·87
	8	0·66	0·73	1·03

* The control cows (nos. 2 and 5) received no thyroxine in period 2.

Administration of thyroxine. A solution of 'thyroxine sodium B.P.' (British Drug Houses Ltd.) containing 1 mg./ml. was made up according to Folley & White (1936). Each day during the thyroxine periods 10 ml. of this solution were injected subcutaneously into the flanks of the cows. Cows 1, 3, 4 and 6 were injected for 28 successive days, and cows 7 and 8 for 32 and 31 successive days respectively.

Methods of analysis. Total N was estimated by the Kjeldahl method, the catalyst being K_2SO_4, $CuSO_4$ and powdered selenium. For estimating N in milk, the samples were weighed and not pipetted. Milk fat was estimated by the Gerber process, and milk phosphatase by the method of Kay & Graham (1933). In the first two experiments the amount of urea plus NH_3 in the urine was determined according to Peters & Van Slyke (1932), and in all three experiments the creatine and creatinine contents of urine were estimated by a modification of Jaffe's picric acid method (Hawk & Bergeim, 1927) using a Spekker absorptiometer.

RESULTS

Pulse rates and milk phosphatase. It was essential for the purpose of this investigation to find out as early in the thyroxine period as possible whether the hormone was showing its usual physiological activity. The two criteria used for this purpose were the effect of thyroxine in enhancing the pulse rate and the rapid diminution which thyroxine produces in the concentration of phosphatase in the milk (Folley & White, 1936). Every day, except Sunday, throughout all three experiments pulse rates were determined by palpation of the plantar arteries of a forelimb, care being taken to ensure that the animals were not excited in any way. During the determination the animals were standing up and either eating hay or ruminating just after having eaten it. Four concurrent determinations were made. From the average results (Table 2) it can be seen that with all the treated animals there was a marked increase in pulse rate during the thyroxine period, whereas with the two controls during the same period no significant increase occurred. Table 2 also shows that the time, which elapsed from the first injection to the day when the pulse rate was maximal, varied from cow to cow. With cow 8 the pulse continued to increase during treatment. With all the other treated cows the pulse had passed its maximum before injection ceased.

Averages of many determinations of milk phosphatase are shown in Table 2. With the two controls there was a tendency for the phosphatase in the milk to increase as lactation advanced, whereas with the treated cows there was the expected substantial decrease during hormone treatment.

Table 2. *The effect of thyroxine on the pulse rate and on the phosphatase content of the milk*

		Pulse rate/min.				Phosphatase in milk*		
			Period 2 (thyroxine)					
Exp. no.	Cow no.	Period 1 (no thyroxine)		Days to maximum†	Period 3 (no thyroxine)	Period 1 (no thyroxine)	Period 2 (thyroxine)	Period 3 (no thyroxine)
1	1	46	65	17	49	68	31	84
	2 (control)	51	47	—	46	90	108	111
	3	59	68	6	52	22	7	43
2	4	65	81	19	66	47	8	39
	5 (control)	64	65	—	63	76	110	106
	6	55	60	13	55	39	8	53
3	7	57	90	29	69	136	40	164
	8	62	83	31	61	82	39	154

* Units of Kay & Graham (1933) multiplied by 100.
† Time elapsing from beginning of treatment to the day when the pulse was maximal.

Milk yield. The milk-yield curves for all eight cows are shown in Fig. 1, and the averages for each period in Table 3. It can readily be seen that with the two controls (nos. 2 and 5) the milk yield tended to decrease gradually over the whole period, whereas with the remaining six cows the milk yield was enhanced from about 2 days after hormone injections began until a few days after they ceased. Owing to the difficulty of judging what the yield would have been had no hormone been given, it is not easy to determine quantitatively the effect of thyroxine on milk yield. From the graphs in Fig. 1, however, it has been estimated that the average enhancement of yield by thyroxine was about 30%, which is comparable to results reported by other workers mentioned in the introduction.

Milk composition. With all the treated animals the yield of milk fat was greatly increased during the thyroxine period. Typical results for one control and one treated animal are shown in Fig. 2. With all the treated animals the increase in the yield of fat persisted longer than that of milk as a whole after thyroxine treatment had ceased. The average values for the fat content of the milk and for the nitrogen content of the fat-free milk from all eight cows, and for the non-fatty solids for two of the cows, are

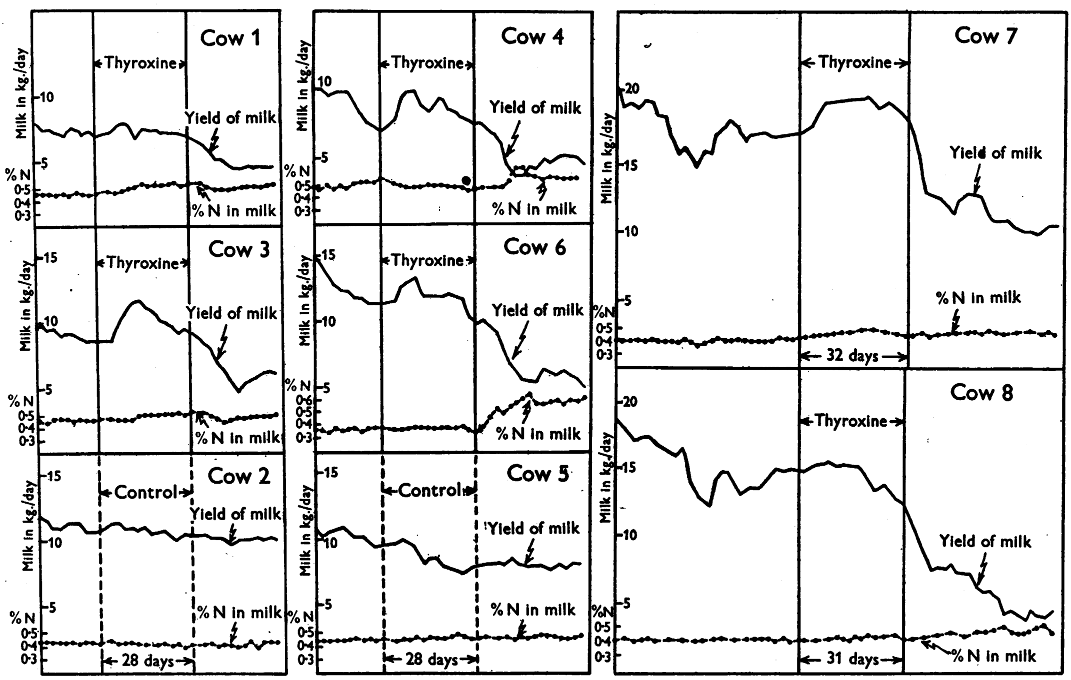

Fig. 1. The effect of thyroxine on milk yield and on the percentage of nitrogen in the milk.

Table 3. *The average yield and composition of the milk produced in each period*

(Thyroxine was given only during period 2 to all cows, with the exception of nos. 2 and 5 which received no hormone at all.)

Exp. no.	Cow no.	Yield of milk (lb./day) Period 1	2	3	Fat content (%) Period 1	2	3	N content of the fat-free milk (%) Period 1	2	3	Solids content of the fat-free milk (%) Period 1	2	3
1	1	7·3	7·3	4·7	4·26	5·65	4·07	0·485	0·529	0·512	—	—	—
	2 (control)	11·2	10·8	10·0	3·63	3·32	3·15	0·451	0·427	0·431	—	—	—
	3	9·3	10·3	6·2	3·79	4·63	3·78	0·484	0·513	0·495	—	—	—
2	4	9·1	8·7	4·7	4·15	4·52	4·38	0·522	0·499	0·563	—	—	—
	5 (control)	10·3	8·5	8·0	2·98	3·10	2·95	0·453	0·477	0·485	—	—	—
	6	12·5	11·6	6·1	4·41	5·19	4·98	0·426	0·504	0·601	—	—	—
3	7	17·6	19·4	12·5	3·56	4·01	3·52	0·434	0·494	0·488	9·11	9·66	9·37
	8	15·2	14·6	6·7	3·70	4·08	4·41	0·441	0·465	0·522	8·77	9·06	9·00

shown in Table 3. Statistical analysis showed that the increases which occurred during hormone treatment were significant.

Body weights. All the animals were weighed at the beginning and end of each period. Each weight recorded was the average of three weighings made at different times on one day (Owen, Smith & Wright, 1943). The weights of the animals at the beginning of the first period of each experiment are shown in Table 4, the changes in weight which occurred during each period being expressed as a percentage of the initial weight. It will be observed that, in contrast to the control cows, all the treated animals lost weight in the thyroxine period, but gained weight again in period 3, after thyroxine injections had ceased. The result of this gain in weight in the final period was that the net loss of weight during the thyroxine and post-thyroxine periods taken together (periods 2 and 3) was of the same order for nearly all the animals whether treated or controls. The only exception was cow 7 which did not show the same degree of recovery in period 3 as the others, although it, like cow 8, was fed the most liberal diet. It should be noted, however, that cow 7 gave a greater increase in the yield of milk fat than cow 8 in the thyroxine period, and that this may have accounted in part for its lower recovery of weight.

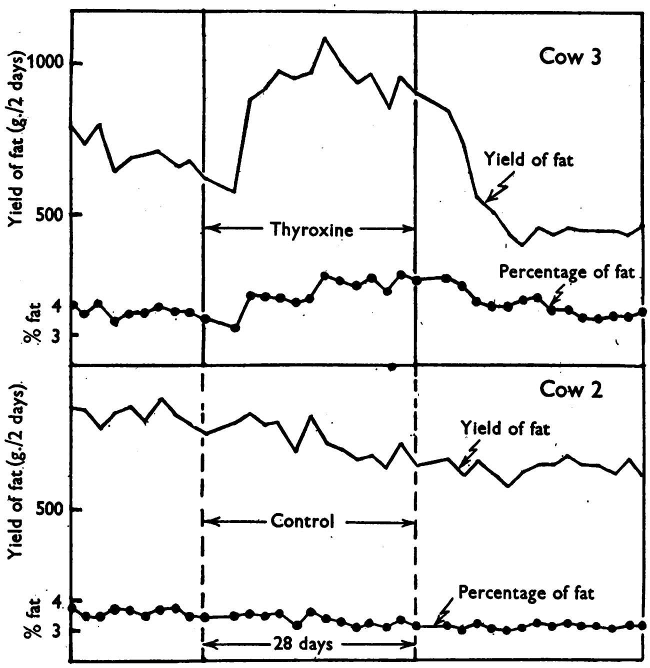

Fig. 2. The effect of thyroxine on the yield and percentage of fat in the milk.

Table 4. *Effect of thyroxine on body weight*

(Thyroxine was given during period 2 to all cows except the controls.)

Exp. no.	Cow no.	Weight at beginning of period 1 (lb.)	Change in weight (lb.) in each period expressed as % of the weight at the beginning of period 1: Period 1 (*a*)	Period 2 (*b*)	Period 3 (*c*)	Change in weight (lb.) in period 2 which was not made good in period 3 (*b*) + (*c*)
1	1	857	−5·4	− 5·8	+ 4·1	−1·7
	2 (control)	817	0·0	+ 2·1	− 4·2	−2·1
	3	872	−0·4	− 6·9	+ 6·3	−0·6
2	4	823	+0·2	− 9·7	+ 8·7	−1·0
	5 (control)	1006	−0·9	+ 2·0	− 1·3	+0·7
	6	945	−0·9	−13·3	+11·1	−2·2
3	7	1007	+0·2	−10·1	+ 3·2	−6·9
	8	1062	+7·5	− 7·8	+ 6·8	−1·0

As is shown in the next paragraph, the nitrogen balances of cows 7 and 8, unlike those of the other treated cows, did not become negative when the cows were given thyroxine. It is, therefore, difficult to relate the loss in weight occurring during thyroxine treatment to any definite metabolic function. It is probable that the decreases of body weight of cows 1, 3, 4 and 6 were due to loss of both protein and fat, whilst the decreases of body weight shown by cows 7 and 8 were due mainly to loss of fat. Catabolism of fat need not parallel that of protein, while loss of protein from the body is known to be sometimes accompanied by retention of water, as, for example, in famine oedema. With ruminants the percentage of food in the gut is about 12 % (Ritzman & Benedict, 1938), so that changes of 'fill' of the cows may have been partly responsible for changes of weight.

Nitrogen metabolism. All foods, including hay, and also milk, urine and faeces, were analyzed for total nitrogen every 2 days. Average results for each period are recorded in Table 5.

Table 5. *A summary of the results required to obtain the nitrogen balances*

(Thyroxine was given during period 2 to all cows except the controls. Results are given in g. N/day.)

Exp. no.	Cow no.	Period	Intake*	Output of N in: Milk	Urine	Faeces	Total output	Balance
1	1	1	153·4	42·3	31·9	69·4	143·6	+ 9·8
		2	129·1	36·3	32·8	63·5	132·6	− 3·5
		3	126·7	23·2	32·4	54·3	109·9	+16·8
	2 (control)	1	161·1	50·2	29·0	69·4	148·6	+12·5
		2	146·7	44·4	35·1	58·5	138·0	+ 8·7
		3	144·3	41·7	40·2	53·2	135·1	+ 9·2
	3	1	157·2	43·7	25·4	63·1	132·2	+25·0
		2	138·1	50·5	32·9	66·1	149·5	−11·4
		3	135·7	29·6	35·4	56·7	121·7	+14·0
2	4	1	166·3	45·6	40·3	64·8	150·7	+15·6
		2	157·7	41·3	42·0	78·8	162·1	− 4·4
		3	151·9	24·8	37·1	69·1	131·0	+20·9
	5 (control)	1	174·0	45·8	55·7	68·8	170·3	+ 3·7
		2	153·4	39·1	48·4	69·6	157·1	− 3·7
		3	146·2	37·6	44·5	67·3	149·4	− 3·2
	6	1	190·0	59·7	58·4	70·7	188·8	+ 1·2
		2	181·2	55·4	55·7	79·7	190·8	− 9·6
		3	176·4	34·7	49·4	70·7	154·8	+21·6
3	7	1	277·2	74·4	71·9	112·0	258·3	+18·9
		2	315·7	93·0	95·9	120·6	309·5	+ 6·2
		3	250·5	56·4	64·5	108·4	229·3	+21·2
	8	1	256·7	66·6	92·3	93·3	252·2	+ 4·5
		2	261·1	64·2	86·6	102·3	253·1	+ 8·0
		3	172·6	30·6	58·3	79·5	168·4	+ 4·2

* Corrected for food refusals which occurred but seldom and were very small.

In Exp. 1, during the thyroxine period, the nitrogen balances for both the treated cows became negative, whereas the nitrogen balance in the control cow remained positive. Of the two treated animals, cow 3 showed the greater stimulation of milk yield by thyroxine, and it also showed the greater negative nitrogen balance (−11·5, as compared with −3·5 g. N/day). After hormone treatment ceased, the nitrogen balances of both the experimental animals became markedly positive. In Exp. 2, the results were very similar, in spite of the fact that the cows were allowed a slightly higher protein intake per gallon of milk. In this experiment even the control cow showed a small negative balance of −3·7 g. N/day in period 2. But, whereas the nitrogen balance of this animal remained almost unchanged in period 3, those of cows 4 and 6 became strongly positive (+20·9 and +21·6 g. N/day), after thyroxine treatment had been discontinued. These positive balances in the last period indicate that the retention of nitrogen after thyroxine treatment was much faster than the loss of nitrogen during treatment. In considering the possible effect of the hormone on the cows' health, it is therefore reasonable to suppose that any ill effects due to increased catabolism during hormone treatment may be offset by the raised anabolism after the treatment is discontinued.

In Exp. 3, in which the allowance of protein per gallon of milk was further increased, the two cows

7 and 8 showed increases in the yields of milk and milk fat which were very similar to those of cow 6 in Exp. 2, and yet their nitrogen balances remained positive throughout the entire experiment. The positive balance for cow 7 was reduced during thyroxine treatment, but increased again after treatment ceased. But with cow 8, which showed a much larger stimulation of milk production than any of the other cows, the positive nitrogen balance was slightly increased during hormone treatment. It may be concluded from these findings that, on normal rations, the increased milk yield produced by 10 mg. thyroxine/day is accompanied by an accelerated protein catabolism, but that this excessive catabolism may be inhibited by increasing the intake of food.

Partition of urinary nitrogen

(1) *Urea plus ammonia.* The proportion of urinary nitrogen excreted as urea plus ammonia was determined for the composite 2-day samples of urine collected from all six cows during the first two experiments. The results showed a constant ratio (60%) of urea plus ammonia to total nitrogen throughout all three periods.

(2) *Creatine and creatinine.* The results for the excretion of creatine and creatinine in Exp. 2 are shown in Fig. 3. The corresponding graphs for the first and third experiments were very similar. No significant change was noted in the creatinine excretion for any of the cows, nor in the creatine excretion of the control animals (e.g. cow 5, Fig. 3). With the treated animals, however, changes in the creatine excretion tended to follow changes in milk yield. Thus, in the thyroxine period, the creatine excretion was first enhanced, and then began to fall some time before thyroxine treatment ceased. After treatment ceased creatine excretion fell rapidly to a very low value, the fall corresponding roughly to that in milk yield. Like the milk yield, the creatine output then increased again. In the third experiment, where the rations were much more liberal and where the nitrogen balance was always positive, the creatine excretion was again maximal during thyroxine treatment and minimal immediately after the treatment ceased, but the changes were smaller with these two cows (particularly with cow 8) than with the animals in the first two experiments in which the nitrogen balances became negative during treatment. If it is supposed that the creatine is of catabolic origin, these variations in the amount excreted are just what would be expected. Stimulation of milk yield might well be associated with increased catabolism, and this would be accompanied by an increased output of creatine. It does not follow, however, that creatine excretion is causally related to milk production, for it is probable that the creatinuria occurring during hormone treatment is merely a result of the general increase in metabolic rate which thyroxine produces in the tissues as a whole.

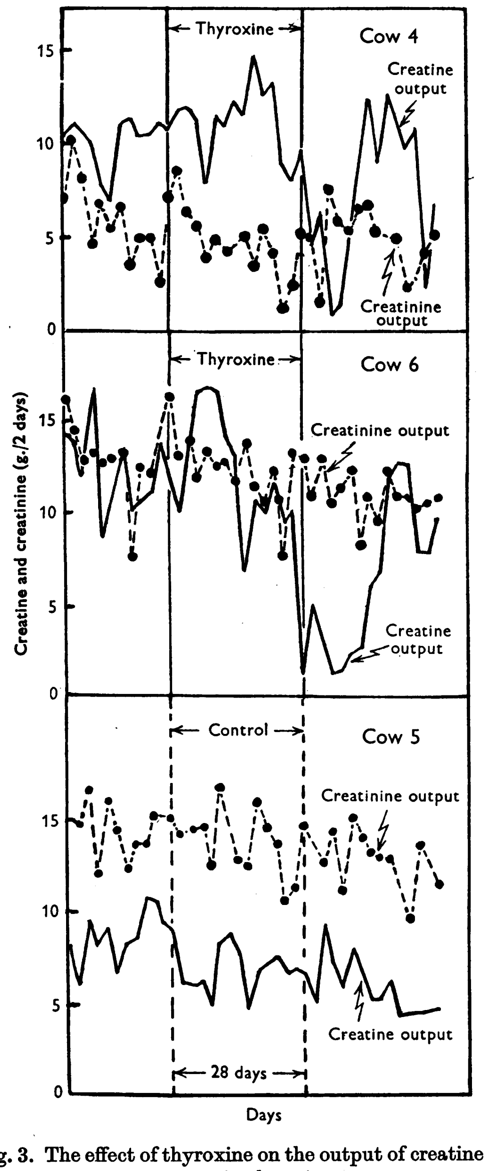

Fig. 3. The effect of thyroxine on the output of creatine and creatinine in the urine.

For ease in comparing the excretion of creatine and creatinine nitrogen, the results have been recorded in Table 6 as percentages of the total urinary nitrogen. The creatinine figures were variable and showed no consistent change which could be related to the hormone treatment. As would be expected from the creatine outputs (Fig. 3), and from the urinary nitrogen outputs (Table 5), the creatine figures for the treated animals tended to be slightly higher during hormone treatment than before it. When thyroxine administration was discontinued, creatine output decreased. This was marked with cows 1, 3, 4 and 6, but not so marked with cows 7 and 8. The same tendency was noted for control cow 2, but not for control cow 5. This difference between the control cows may be related to the fact that cow 5 was fed at a slightly higher level than cow 2. For the best fed cows (7 and 8) the percentage of total urinary nitrogen excreted, as creatine and creatinine, was much smaller than for the other cows. This was due to the fact that the total amount of nitrogen excreted in the urine was naturally higher for the best-fed animals than for the others (Table 5).

Table 6. *Output of creatine and creatinine (expressed as percentage of total urinary nitrogen*

		Creatine Period			Creatinine Period		
Exp. no.	Cow no.	1	2	3	1	2	3
1	1	9·5	10·5	6·6	4·0	4·4	3·5
	2 (control)	6·1	6·7	5·5	6·4	6·4	5·1
	3	6·8	8·8	4·6	11·1	8·2	7·2
2	4	7·1	7·6	5·4	4·2	3·1	3·9
	5 (control)	4·4	4·1	4·4	7·1	8·0	7·8
	6	5·9	5·8	3·7	6·2	6·1	6·2
3	7	2·3	2·4	2·0	2·9	3·3	3·6
	8	1·0	1·5	1·1	3·4	4·5	5·1

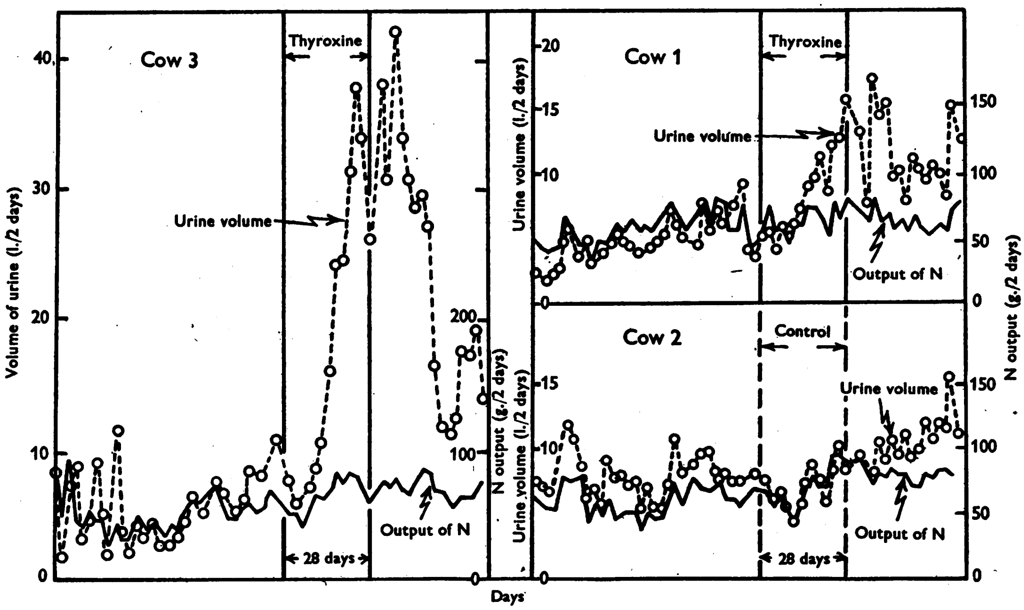

Fig. 4. The effect of thyroxine on the volume of urine and on the output of total nitrogen in the urine.

The diuretic effect

The volume of urine and the urinary nitrogen excreted per day by the cows in the first experiment are shown in Fig. 4. It will be noted that for the control cow 2 there was a reasonably close parallelism between the volume and the amount of urinary nitrogen throughout the pre-thyroxine and thyroxine periods. This parallelism also existed with cows 1 and 3 before hormone treatment, but, some days after treatment began, a substantial increase in volume occurred. An increase in volume was shown at this stage by all the experimental cows, but not by either of the controls. This may have been caused in part by the cows using water to disperse some of the extra heat generated in their tissues when thyroxine increased the metabolic rate, or it may be that thyroxine raised the activity of the kidneys either directly or by stimulating the secretion of a diuretic hormone. The very large increase in urinary volume noted for cow 3 (Fig. 4) was exceptional, the increase in volume with the other experimental animals being of the order of that shown for cow 1. It is not known why the increase with cow 3 was so large.

The effect of thyroxine on the utilization of food

Apparent digestibility of dietary nitrogen. An attempt is made to assess the effect of thyroxine on the utilization of food by calculating the average values for apparent digestibility of the dietary nitrogen and the efficiency of its conversion to milk nitrogen in each of the three periods (Table 7). In Exp. 1 the apparent digestibility with control cow 2 increased as the experiment progressed, whereas with the treated animals there was a substantial decrease during thyroxine treatment. In Exp. 2 the control animal (no. 5) showed a progressive decrease in the apparent digestibility of its dietary nitrogen. The treated animals, on the other hand, like the treated animals in the first experiment, showed a decrease during hormone treatment, which changed to an increase when hormone treatment ceased. In Exp. 3 there was no significant difference in the results for periods 1 and 2, but when thyroxine treatment ceased the apparent digestibility decreased. This difference between the changes noted in the first two experiments and those in the third is probably associated with the much higher level of feeding in the last experiment. It may be concluded that at the lower levels of feeding the apparent digestibility of the dietary nitrogen tends to be decreased when thyroxine is administered. Estimation of the moisture content of the faeces throughout the entire experiment showed that during thyroxine treatment the faeces were more moist. They were also obviously softer and more liquid than in the control periods. This might tend to cause the contents of the alimentary tract to be retained for a shorter time during thyroxine treatment than is usually the case, and this, in turn, might cause a reduction in the amount of nitrogen absorbed. With cows 7 and 8 the more rapid passage of food caused by thyroxine treatment would tend to offset the effect of the more liberal feeding.

Table 7. *The apparent digestibility of the dietary nitrogen and the efficiency of conversion of the dietary nitrogen to milk nitrogen*

(The apparent digestibility is defined as $100\,\frac{(\text{Intake N} - \text{faecal N})}{\text{Intake N}}$; the conversion of dietary N to milk N is expressed as the ratio $\frac{\text{Milk N} \times 100}{\text{Intake N} - \text{faecal N}}$.)

		Apparent digestibility Period			Conversion of dietary N to milk N Period		
Exp. no.	Cow no.	1	2	3	1	2	3
1	1	55	51	57	50	55	32
	2 (control)	57	60	63	65	50	46
	3	60	52	58	46	71	38
2	4	61	50	55	45	52	30
	5 (control)	61	55	54	44	47	48
	6	63	56	60	50	55	33
3	7	59	62	57	51	50	47
	8	64	60	54	39	40	33

Conversion of dietary nitrogen to milk nitrogen. The results in Table 7 show that in the first two experiments thyroxine caused a marked increase in the apparent efficiency with which the dietary nitrogen was converted to milk nitrogen. When hormone treatment ceased an even more marked change, in this case a decrease in apparent efficiency, occurred. Of the two control cows (2 and 5) one behaved differently from the other in this respect. The efficiency of conversion decreased with cow 2 and increased with cow 5 as the experiment progressed, but they both differed from the experimental animals in not showing a maximum in period 2. In Exp. 3 the better fed cows (7 and 8) did not show any significant change in efficiency of conversion when thyroxine was given, in spite of the larger increases in milk yield. They also showed smaller decreases in efficiency of conversion when thyroxine was discontinued.

DISCUSSION

The experiments reported show that, under conditions of controlled food intake, the effect of thyroxine in stimulating the yield of milk can be attributed mainly to an increase in catabolism. The metabolic rate, as measured by the pulse rate, is much accelerated, so that weight is lost and nitrogen balance becomes negative. However, negative nitrogen balances during thyroxine treatment can be inhibited by a more liberal allowance of food. This diminution of catabolism as a result of increasing food intake recalls a similar phenomenon, reported by Cuthbertson (1942), Croft & Peters (1945) and Taylor (1943), who found that large negative nitrogen balances resulting from trauma could be reversed by increasing the food intake.

The effects of thyroxine in increasing catabolism were reversed during the period following its discontinuance. Nitrogen retention increased markedly, the pulse rate reverted to somewhat less than its pretreatment level, and the graphs for the yields of milk and milk fat showed distinct minima. During this last period of the experiments tissue anabolism evidently took precedence over milk secretion in its claim for available nutrients.

The foodstuffs used in these experiments were, with the exception of groundnut, such as can readily be grown in Britain. It might, therefore, at times be economic to obtain a temporary increase of the milk supply by the feeding of iodinated casein, the action of which is very similar to that of thyroxine. Although such feeding would temporarily increase catabolism, any consequent ill effects would be largely overcome by the stimulus to anabolism which occurs when the treatment is discontinued. Any subsequent loss of efficiency by the cow would have to be balanced against the temporary gain of milk yield without any increase in the number of cows in the herd, in the man-hours or in the materials other than foodstuffs required for its production.

SUMMARY

1. The effect of injecting 10 mg. thyroxine/day for 4 weeks into cows at three different levels of food intake has been investigated. The resultant increase in milk yield was accompanied by an increase in pulse rate, by loss of weight, by markedly negative nitrogen balance and by an increase in the excretion of water and creatine in the urine. The percentage of fat in the milk was increased and small but statistically significant increases were observed in the percentage of solids and of nitrogen in the fat-free milk.

2. Thyroxine appeared to stimulate lactation by increasing the cows' catabolism, and this resulted in negative nitrogen balances.

3. The negative nitrogen balances could be inhibited by increasing the intake of food.

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The Effect of Thyroxine on the Metabolism of Lactating Cows

2. CALCIUM AND PHOSPHORUS METABOLISM

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In the previous paper (Owen, 1948), experiments have been described on the effect of thyroxine injections on the nitrogen metabolism of lactating cows. During these experiments, data for the calculation of calcium balances were obtained for all the cows, and data for phosphorus balances for two of them. The purpose of the present communication is to report the effect of thyroxine on the calcium and phosphorus contents of the milk, and also on the calcium and phosphorus metabolism of the cows when thyroxine was administered with the object of increasing the milk yield.

EXPERIMENTAL

The general plan of the experiments and the nature of the rations have been described already (Owen, 1948). There were three experiments, each comprising three periods. The intention was to have three cows in each experiment, but in