Kodicek, E. & Pepper, C. R. (1948). *J. gen. Microbiol.* **2**, 292.
Krehl, W. A., Elvehjem, C. A. & Strong, F. M. (1944). *J. biol. Chem.* **156**, 13.
Lardy, H. A., Potter, R. L. & Burris, R. H. (1949). *J. biol. Chem.* **179**, 721.
Lardy, H. A., Potter, R. L. & Elvehjem, C. A. (1947). *J. biol. Chem.* **169**, 451.
Lichstein, H. C. & Christman, J. F. (1948). *J. biol. Chem.* **175**, 649.
Lichstein, H. C. & Umbreit, W. W. (1947*a*). *J. biol. Chem.* **170**, 329.
Lichstein, H. C. & Umbreit, W. W. (1947*b*). *J. biol. Chem.* **170**, 423.
Lipmann, F., Kaplan, N. O., Novelli, G. D., Tuttle, L. C. & Guirard, B. M. (1947). *J. biol. Chem.* **167**, 869.
McIlwain, H. & Stanley, D. A. (1948). *J. gen. Microbiol.* **2**, xii.
Ochoa, S., Mehler, A., Blanchard, M. L., Jukes, T. H., Hoffmann, C. E. & Regan, M. (1947). *J. biol. Chem.* **170**, 413.
Price, S. A. & Graves, H. C. H. (1944). *Nature, Lond.*, **153**, 461.
Shive, W. & Rogers, L. L. (1947). *J. biol. Chem.* **169**, 453.
Sohonie, K. & Misra, U. C. (1950). *Brit. J. Nutrit.* **4**, 134.
Williams, V. R. & Fieger, E. A. (1946). *J. biol. Chem.* **166**, 335.
Williams, W. L., Broquist, H. P. & Snell, E. E. (1947). *J. biol. Chem.* **170**, 619.
Wood, E. C. (1945). *Nature, Lond.*, **155**, 632.
Wood, E. C. (1946). *Analyst*, **71**, 1.

Factors Affecting the Utilization of Food by Dairy Cows

5. The Digestibility and Rate of Passage of Foods during L-Thyroxine Administration

BY C. C. BALCH, D. A. BALCH, S. BARTLETT, V. W. JOHNSON AND S. J. ROWLAND
National Institute for Research in Dairying, University of Reading

(*Received* 29 *August* 1951)

It is well known that the administration of thyroid-active substances to lactating cows usually stimulates milk secretion and, in this way, may affect the efficiency of food utilization. Until recently iodinated protein was the cheapest and most suitable thyroid-active substance available, but synthetically produced L-thyroxine, given by mouth, now appears to be the most suitable material (Bailey, Bartlett & Folley, 1949). The administration of thyroid-active substances raises the metabolic rate and increases the nutritive requirements of cows. The literature on this subject has been reviewed by Blaxter, Reineke, Crampton & Petersen (1949), and further results have been reported by Moustgaard & Thorbek (1949). The experiment described in this paper was an attempt to find whether this increased requirement is met, even partly, by a more efficient digestion of available food or whether the cows can obtain additional nutrients only by eating more food or utilizing body reserves.

The administration of thyroid-active materials is known to increase the rate of stomach emptying and intestinal motility in non-ruminants (see review by Ivy, 1930). In cows the administration of iodinated protein (Blaxter, 1946) and of thyroxine (Owen, 1948) is known to produce moister faeces, and the same effect has been observed in sheep given heavy doses of iodinated casein (Blaxter, 1948); this has sometimes been thought to signify a faster rate of passage of food. The effect of an in-

creased rate of passage on digestive efficiency would depend on simultaneous changes in the rate of production of the digestive secretions and on the rate of absorption of the products of digestion; if these rates were also increased, the digestibility of the food might not be affected. It was shown by Fink (1944) that thyroid extracts cause an increased production of digestive secretions in the jejunum of the dog, and Althausen & Stockholm (1938) found that in the rat thyroidectomy decreases dextrose absorption in the digestive tract and that the administration of thyroxine increases the rate of absorption of dextrose, galactose, xylose and oleic acid but not of alanine. Blaxter (1948) found that heavy doses of iodinated casein depress the digestibility of the dry matter and crude protein of mixed diets of hay, oats and flaked maize in sheep fed according to standard (Kellner, 1907). Owen (1948) found an increased faecal excretion of nitrogen during the administration of thyroxine to cows on a low plane of nutrition, but not to cows on a high plane of nutrition, and tentatively suggested that the increased excretion of nitrogen might be due partly to a more rapid rate of passage preventing optimum absorption. Results are here reported of an experiment in which the effect of L-thyroxine on digestibility and rate of passage was determined in lactating cows receiving an ample diet.

METHODS

Cows and their treatment. For the experiment, which lasted 10 weeks and was divided into two main parts, four Shorthorn cows in declining lactation were selected from the Institute herd.

The cows were given the same diet of hay and concentrates throughout, but during the second part of the experiment, which included the 5th–10th weeks, they were each given orally 100 mg L-thyroxine/day. (This was later reduced in two cows, see p. 358.) During the 1st week the intake of hay was adjusted to a level almost sufficient to satisfy appetite, and concentrates were fed at the rate of 0·4 kg/kg milk produced in the previous week. In the 2nd week the cows were fed the same amount of hay, and concentrates at the rate of 0·4 kg/kg milk produced in the 1st week plus an additional 1·8 kg concentrates/cow/day. These amounts were given throughout the remainder of the experiment (Table 1). The hay was of a coarse type containing little clover, and

Table 1. *Foods offered to cows in weeks 2–10 inclusive*

Cow	Hay (kg/day)	Concentrates (kg/day)
A	9·1	7·3
B	7·3	7·3
C	5·4	7·8
D	9·1	8·2

with Italian ryegrass (*Lolium italicum*) predominating. The concentrate mixture contained dredge corn (oats and beans) 30, wheat bran 10, coconut meal 20, palm-kernel cake 20, decorticated cottonseed cake 10, and decorticated groundnut cake 10, parts with the addition of 2% of a commercial mineral mixture. Each animal had access to a salt lick. These diets proved ample to satisfy appetite, but food was refused on a few occasions.

Thyroxine administration. During the 5th week all the cows were given L-thyroxine*. The dose was successively 25, 50, 75 and 100 mg on the first 4 days of the week and continued at 100 mg daily until the 8th week when it became obvious that this was above the optimum dose for cows B and C, which were showing signs of slight distress; they had very high heart rates and were restless. These cows were accordingly given 75 mg/day in the 8th week and subsequently. In the 10th week all the doses were gradually reduced to nil.

Measurements of the digestibility and rate of passage of the food. Measurements of the digestibility of the diet and of the rate of passage of hay through the digestive tract were made in two collection periods of 14 days. These periods occupied weeks 3–4 and 8–9 during the control and thyroxine treatments respectively. By arranging the treatments in this way the results were not affected by any after-effects of thyroxine treatment.

The digestibility trials and measurements of the rate of passage of hay were essentially similar to those described by Balch (1950) for collection periods of 10 days. Faeces were collected in rubber bags supported on a harness worn by the cows, and separated from urine by a special separating device also fixed to the harness (Balch, Bartlett & Johnson, 1951). By using a 14-day collection period it was possible to calculate digestibility coefficients in each of the 2 weeks, and this gave an indication of the accuracy of the method. The longer period also made possible a check of the accuracy of the determinations of the rate of passage of hay. This was done by giving small meals of hay stained with magenta on the 1st day, and of hay stained with brilliant green on the 4th day, of each collection period. The method of sampling faeces, counting stained particles in the samples and plotting excretion curves was described earlier by Balch (1950).

Other measurements. Throughout the experiment, records of the amount of water drunk by the cows, of their heart rates and rectal temperatures were made daily, and the cows were weighed at intervals.

The cows were milked twice daily by machine. Twice weekly, determinations of the content of total solids, by the gravimetric method, fat by the Gerber method and solids-not-fat by difference, were made on samples of milk from four consecutive milkings bulked in proportion to the yield at those milkings.

RESULTS

Effect of thyroxine. Measurement of the heart rate, rectal temperature and of the amount of water drunk showed clearly that the daily administration of 100 mg thyroxine per cow produced a marked rise in metabolism (Fig. 1). The heart rate of every cow increased by 10–20 beats/min and began to fall as the dose of thyroxine was reduced. Three of the four cows drank more water during thyroxine administration. Fig. 1 also shows that the rate of decline in milk yield was altered in all the cows. The yield rose for 2 weeks before falling at about the same rate of decline as in the control period. During the control period the weight of the cows changed little, apart from that of cow A, which rose, but while thyroxine was being given all the cows lost weight, the weekly losses varying from 2·4 to 8·3 kg/cow (Table 2).

* As cubes containing 6 g oatmeal and 25 mg monosodium L-thyroxine.

Digestibility coefficients. The mean digestibility coefficients in the 14-day collection periods are given in Table 3. There were small differences between the coefficients for

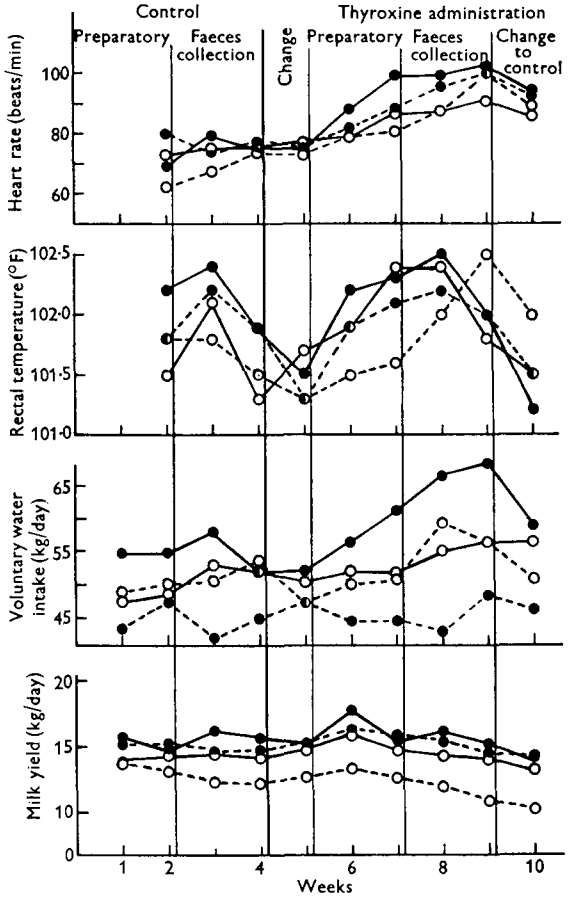

Fig. 1. Effect of thyroxine administration on the heart rate, rectal temperature, voluntary water intake, and milk yield of cows. Weekly mean values of daily observations are shown for cows A, O- - - -O; B, O——O; C, ●- - - -●; and D, ●——●.

Table 2. *Weights of cows (kg)*

Cow	Beginning of experiment	End of part 1 (control)	End of part 2 (thyroxine administration)	Mean weekly change: Control period	Mean weekly change: Thyroxine period
A	617	632	583	+4·3	−2·4
B	499	497	475	−0·6	−4·0
C	495	492	469	−0·9	−4·3
D	623	623	580	0	−8·3

individual cows, due in part to variations in the proportion of hay and concentrates given to the cows. However, in any one cow the differences between values for different weeks of the same collection period were almost invariably considerably greater than the differences between the mean values for the two whole collection

periods and use of the *t* test showed that the probability of any differences due to treatment being greater than the differences due to week-to-week variation was not significant. The greatest differences between the treatments were observed in the digestibility of crude fibre, but here the variation between different weeks of the same collection period was also greatest.

Table 3. *Effect of daily administration of* 100 *mg thyroxine/cow on the digestibility of a mixed diet of hay and concentrates*

(Mean values for four cows)

	Digestibility (%)		
Nutrient	Control period	Thyroxine period	Change due to thyroxine
Dry matter	62·8	63·8	+1·0
Crude protein	67·7	68·8	+1·1
Ether extract	82·9	80·9	−2·0
N-free extract	68·1	68·4	+0·3
Crude fibre	51·3	54·3	+3·0

Table 4. *Time* (*h*) *necessary for the first appearance in the faeces of the cows of residues from a meal of stained hay*

	Control period		Thyroxine period	
Cow	Red hay	Green hay	Red hay	Green hay
A	16	16	16	16
B	12	12	12	12
C	16	12	12	12
D	16	16	16	16

Rate of passage of hay through the cow. The time of the initial appearance of stained residues in the faeces was remarkably constant and was unaffected by the administration of thyroxine (Table 4). The first appearance of residues from stained food in the faeces of cows B and C was always observed in the samples of faeces taken 12 h after feeding, with the exception of red hay in cow C during the control period which first appeared 16 h after feeding. Excretion from cows A and D was spread over a longer period than excretion from cows C and B (Table 4), and residues from both coloured hays were invariably first detected in samples of faeces which accumulated in the period 12–16 h after feeding.

Details of the further progress of excretion of undigested stained hay particles are shown by excretion curves in Fig. 2. The time required for excretion of 5% of the total stained particles excreted in 240 h, which will be called the 5% excretion time, varied more than the time of the initial appearance of the particles in the faeces (Table 5). The differences suggest that the 5% excretion time was less when the cows were receiving thyroxine, but it is unlikely that they were significant. It has been shown (Balch, 1950) that the first appearance of stained foods in the faeces, whether actually determined, as in Table 4, or judged by the time required for the excretion of the first 5% of the total undigested particles, as in Table 5, is indicative of the time required for the excretion of food that has left the reticulo-rumen. Therefore, it can

be concluded that the administration of thyroxine to milking cows did not markedly change the total time required for food residues to pass from the reticulo-rumen to the faeces.

Table 5. *Time (h) required for excretion by the cows of undigested residues from stained hay*

Period	Proportion of total residues from stained hay (%)	Cow A		Cow B		Cow C		Cow D	
		Red hay	Green hay	Red hay	Green hay	Red hay	Green hay	Red hay	Green hay
Control	5*	29	29	21	21	30	30	24	22
	80*	107	124	91	100	138	126	101	90
	80−5*	78	95	70	79	108	96	77	68
Thyroxine	5*	23	24	21	21	26	30	21	21
	80*	90	100	93	100	126	117	82	86
	80−5*	67	76	72	79	100	87	61	65

* For explanation of these indices of the rate of excretion, see pp. 360, 361.

Table 6. *Effect of* L-*thyroxine on the dry-matter content of the total intake and of the faeces of the cows*

Cow	Intake (%)*			Faeces (%)		
	Control period	Thyroxine period	Change due to thyroxine	Control period	Thyroxine period	Change due to thyroxine
A	20·5	18·3	−2·2	17·2	16·2	−1·0
B	18·7	17·6	−1·1	15·4	14·9	−0·5
C	20·1	19·2	−0·9	18·4	16·8	−1·6
D	20·8	17·5	−3·3	15·4	14·4	−1·0
Mean	20·0	18·1	−1·9	16·6	15·6	−1·0

* $\frac{\text{Dry-matter intake (kg)} + \text{water intake (kg)}}{\text{Water intake (kg)}} \times 100.$

The moisture content of faeces has sometimes been used as an indication of the rate of passage of food. If this were justified it would probably apply particularly to the rate of passage of food residues through the intestine. In the present experiment the administration of thyroxine caused a decrease in the percentage of dry matter in the faeces of every cow (Table 6). On average the dry-matter content of the faeces fell from 16·6 to 15·6%. This decrease was presumably linked to the raised intake of water during thyroxine administration (Fig. 1) and the resultant fall in the dry-matter content of the total intake (Table 6) but, as has been shown above, it was not accompanied by any change in the index of the rate of passage of food from the reticulo-rumen to the faeces.

The spread of excretion curves, of the type shown in Fig. 2, is indicative of the rate of passage of foods through the reticulo-rumen, and an index of this spread is obtained by taking the difference between the times required for 5 and 80% of the total undigested stained particles to be excreted (Balch, 1950). This will be referred to as the '80−5% excretion time'. Values for the spread of the excretion curves are given in Table 5. The mean time required for the excretion of 80−5% of undigested

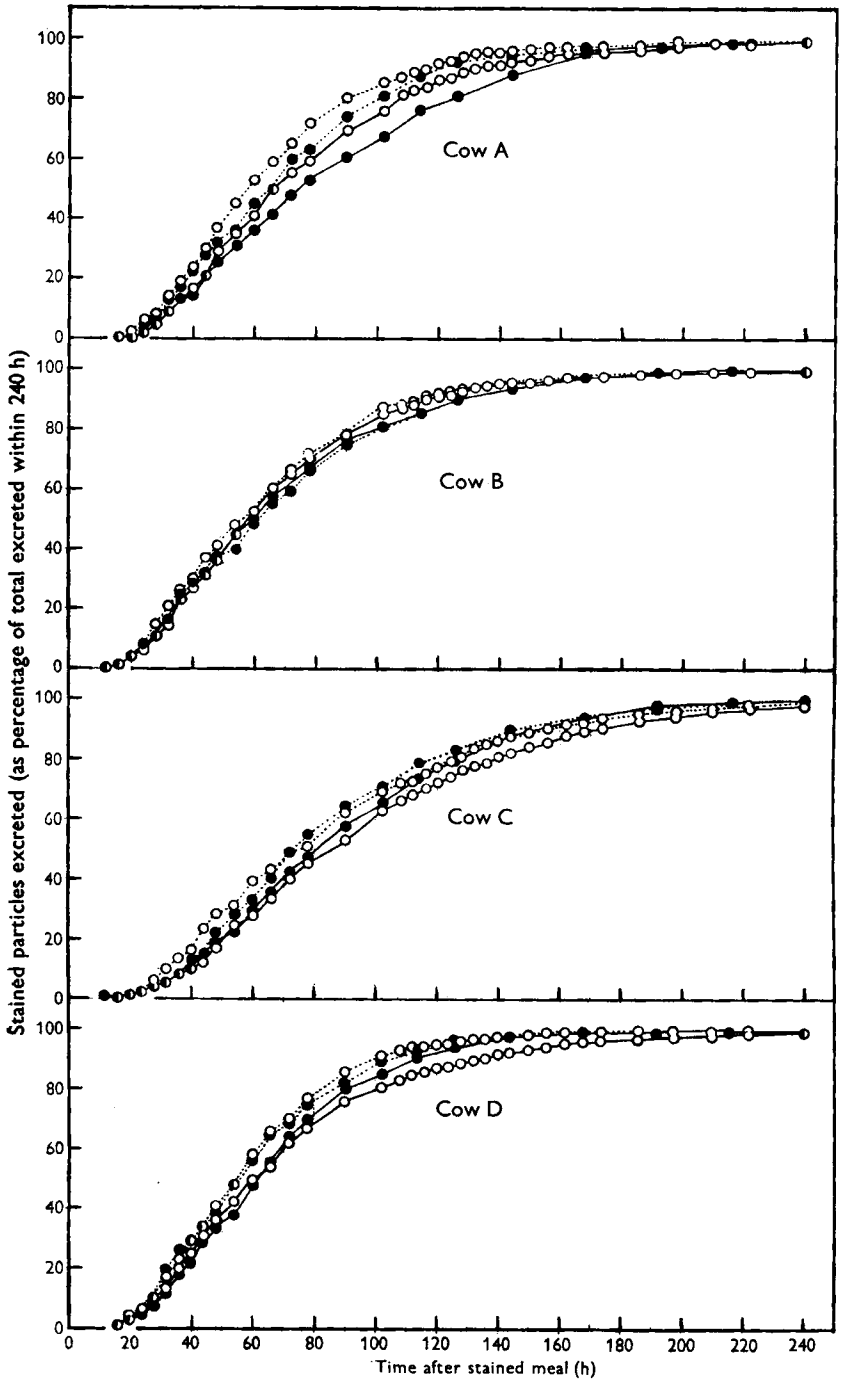

Fig. 2. Values for the excretion of undigested particles (shown as the percentage of the total stained particles excreted within 240 h) of a meal of stained hay in four cows during the control period and period of thyroxine administration. O——O, control period, hay stained red with magenta; ●——●, control period, hay stained green with brilliant green; O- - -O, thyroxine period, hay stained red with magenta; ●- - -●, thyroxine period, hay stained green with brilliant green.

residues of stained hay was 83·9 h in the control period and 75·9 h when the cows received thyroxine. Use of the *t* test showed that the difference between these means was significantly greater at the 5% level than the difference due to errors in measurement, as shown by the difference between values for hay stained red and green.

It therefore seems that, as a result of the administration of thyroxine, food residues tended to be excreted slightly faster than is normal; the data suggest that this acceleration of rate of passage took place in the reticulo-rumen. There was, however, consider-

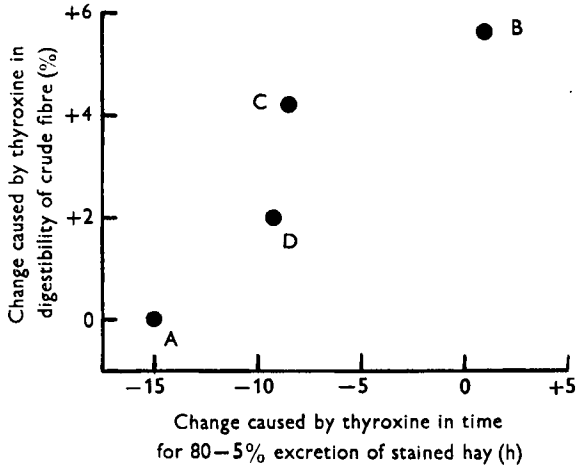

Fig. 3. Relationship between changes in the digestibility of crude fibre and changes in the time required for the excretion of 80−5% of the residues from small meals of stained hay following thyroxine administration to cows A, B, C and D. (For explanation of the 80−5% index of excretion see p. 361.)

able variation in the extent of the faster excretion between the cows, and in one cow the rate of excretion appeared to be unchanged by thyroxine.

Between-cow variations in the changes in the digestibility of crude fibre and the index of the rate of passage of foods through the reticulo-rumen bore a positive relationship (Fig. 3). The significance of this relationship cannot be proved, but it is tempting to suggest that the digestibility of crude fibre was raised in all the cows provided there was not a compensating increase in the rate of passage of the food.

Composition of the milk. Weekly mean values for the composition of the milk of the four cows are given in Fig. 4. In each cow the fat content of the milk rose steadily throughout the 5 weeks of thyroxine administration and dropped as the dose was reduced. The mean solids-not-fat content of the milk increased by 0·1–0·2%. These values are typical of effects of the administration of thyroid-active material to stall-fed cows (Bartlett, Rowland & Thompson, 1949).

DISCUSSION

Changes in the live weight, heart rate, rectal temperature, water intake and milk composition provide ample assurance that the metabolism of the four cows was considerably stimulated during the 5 weeks of thyroxine administration.

The addition of 100 mg thyroxine to the daily concentrate allowance of each cow caused no change in the digestibility of dry matter, or of any of the constituents of the mixed diets of hay and concentrates, nor was there any consistent change in the rate at which the hay passed through the digestive tract.

The effect of thyroxine on the digestibility coefficients for crude protein appears to be in agreement with the work of Owen (1948) who found that the daily intravenous administration of 10 mg thyroxine did not alter the apparent digestibility of dietary

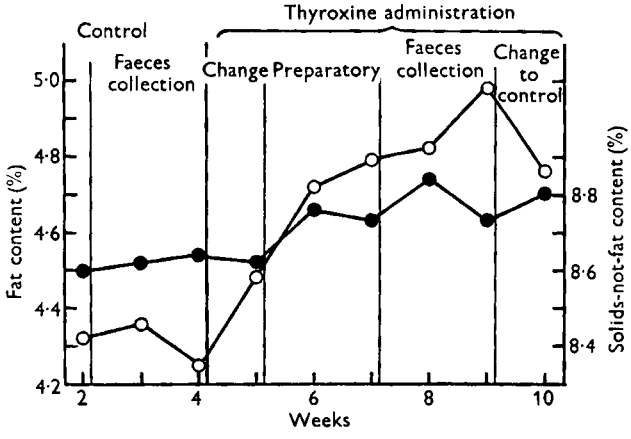

Fig. 4. Effect of thyroxine administration on the fat, ○——○, and solids-not-fat, ●——●, content of milk. Values are weekly means for cows A, B, C and D.

nitrogen in amply fed cows, although if the cows were fed at a lower plane of nutrition the apparent digestibility of dietary nitrogen fell. Cows in the present experiment were fed at a level at least as high as the high level of Owen (1948).

It is probable that the increase in faecal nitrogen and also, therefore, the fall in the apparent digestibility of crude protein, resulting from the administration of thyroid-active substances to cows (Owen, 1948) or sheep (Blaxter, 1948) fed at or below standard requirements, is due to an increase in the metabolic faecal nitrogen resulting from an increased katabolism (Owen, 1948).

Since there was no change in the digestibility of food during thyroxine administration it seems that the cows were depending on surplus food intake or loss of body reserves for their extra nutritional requirements and, in fact, there was some indication that a loss of body-weight occurred even in cows receiving ample food.

The water consumption of cows rose 5–20% during the period of thyroxine administration. This is hardly unexpected in view of the large increases in secretion of urine observed by Owen during thyroxine administration. A possible effect of the rise in water intake was a mean fall in the dry-matter content of the faeces from 16·6 to 15·6%, observed in the present experiment. Owen also observed a fall in the dry-matter content of faeces. It is probable that this rise in water intake slightly lowered the average dry-matter content of the reticulo-ruminal contents. Under such conditions there is reason to expect a more rapid breakdown of fibre in the reticulo-rumen (Balch & Johnson, 1950). No significance can be attached to the positive relationship

that appeared to exist during thyroxine administration between the changes in the digestibility of crude fibre and the rate of passage of hay through the reticulo-rumen. It is tentatively suggested, however, that more fluid conditions in the reticulo-rumen raised the digestibility of crude fibre and that in some of the cows there was a simultaneous increase in the rate of passage of foods, which had the opposite effect.

SUMMARY

1. The oral administration of 100 mg L-thyroxine daily to each of four Shorthorn cows caused increases in metabolism evident as increases in the heart rate, body temperature and water consumption and as changes in the composition of the milk.

2. Thyroxine administration caused no significant changes in the digestibility of the dry matter, crude protein, ether-extractable substances, crude fibre or nitrogen-free extract of an ample diet of hay and concentrates.

3. Thyroxine administration caused no consistent change in the rate of passage of foods through the digestive tract. There was evidence, however, that in three of the four cows foods passed slightly more rapidly through the reticulo-rumen, but the rate of passage of food through the remainder of the gut was unchanged.

4. Results suggest that the extra nutritive requirements of cows given thyroxine can be met only by increased food intake or loss of body reserves and not by an increased efficiency of digestion. In spite of ample feeding the cows lost on the average 4·8 kg a week.

5. The voluntary water intake rose during thyroxine administration. The possible effect of this factor and of the small changes in rate of passage is discussed in relation to the digestion of crude fibre in the reticulo-rumen.

Thanks are due to Mr J. Elton for his help with the handling and management of the cows and to Mr A. Wagstaff and Miss R. Thorner for analysis of the milk.

REFERENCES

Althausen, T. L. & Stockholm, M. (1938). *Amer. J. Physiol.* **123**, 577.
Bailey, G. L., Bartlett, S. & Folley, S. J. (1949). *Nature, Lond.*, **163**, 800.
Balch, C. C. (1950). *Brit. J. Nutrit.* **4**, 361.
Balch, C. C., Bartlett, S. & Johnson, V. W. (1951). *J. agric. Sci.* **41**, 98.
Balch, C. C. & Johnson, V. W. (1950). *Brit. J. Nutrit.* **4**, 389.
Bartlett, S., Rowland, S. J. & Thompson, S. Y. (1949). *Int. Dairy Congr.* XII. *Stockholm.* **1**, 102.
Blaxter, K. L. (1946). *J. agric. Sci.* **36**, 117.
Blaxter, K. L. (1948). *J. agric. Sci.* **38**, 1.
Blaxter, K. L., Reineke, E. P., Crampton, E. W. & Petersen, W. E. (1949). *J. Anim. Sci.* **8**, 307.
Fink, K. (1944). *Amer. J. Physiol.* **141**, 598.
Ivy, A. C. (1930). *Physiol. Rev.* **10**, 282.
Kellner, O. (1907). *Die Ernährung der Landwirtschaftlichen Nutztiere*, 4th ed. Berlin: Paul Taray.
Moustgaard, J. & Thorbek, G. (1949). *Beretn. Forsøgslab. Kbh.* no. 240.
Owen, E. C. (1948). *Biochem. J.* **43**, 235.