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### Use of L-Thyroxine by Mouth for Stimulating Milk Secretion in Lactating Cows

SINCE it was first unequivocally shown that the milk yield of lactating cows could be increased by feeding dried thyroid gland<sup>1</sup> or injecting thyroxine<sup>2,3</sup>, many experiments (see Reineke<sup>4</sup> for review of some of them) have been carried out on the practical use of thyroid-active substances for increasing the milk yield of cows over limited periods of time. Dried thyroid gland and, more recently, iodo-casein (an artificially prepared thyroid-active protein) have been preferred to synthetic thyroxine for this purpose, because of the high cost of the latter and the belief that its activity was not great by the oral route.

In any event, the galactopoietic effects of thyroxine administered to cows by mouth have not yet, so far as we know, been investigated. However, the recent development of new methods for the synthesis, first of racemic thyroxine<sup>5</sup>, and later of L-thyroxine<sup>6</sup>, which holds out considerable promise that thyroxine will eventually be made available on a large scale at a cost low enough to compete with iodo-casein, has now prompted an investigation of the effects of thyroxine, given by mouth, on the milk yield of cows in declining lactation.

Dose/cow/day	Milk yield increase (lb./cow/day)		Heart-rate increase (beats/cow/min.)	
	after 2 weeks	after 3 weeks	after 2 weeks	after 3 weeks
25 mgm. L-thyroxine	1.5	1.6	1.8	5.2
50 mgm. "	3.2	3.6	6.2	8.7
100 mgm. "	6.2	5.9	13.5	15.5
150 mgm. "	6.3	6.3	16.9	21.5
15 gm. iodo-casein	4.9	4.3	7.4	11.2

Forty-eight cows in equal numbers on two farms, comprising eight blocks each of six matched cows, that is, six treatment groups, were used in an experiment involving the feeding of L-thyroxine (as sodium salt) at four dose-levels, iodo-casein at one, and a control group. The thyroxine, incorporated with oatmeal and made into tablets each containing 25 mgm., was fed twice daily for 21 days. The responses given in the accompanying table were calculated from the means of readings for the 12th, 13th and 14th days, and the 19th, 20th and 21st days respectively. In the case of milk yield, the figures for the three days immediately before treatment started were used as a standard of comparison, the responses being calculated by the formula: (milk yield of treated cows in treatment period — milk yield

of control cows in treatment period) — (milk yield of treated cows in control period — milk yield of control cows in control period).

It will be seen that at the three lower dose-levels of thyroxine graded responses were obtained both with milk yield and heart-rate; but 150 mgm. appeared to be an overdose, as evidenced by slight sweating of a few cows after fourteen days. The 15 gm. of iodo-casein, which was chosen as the optimum dose of that preparation, was estimated by linear interpolation to be equivalent to 60–78 mgm. of L-thyroxine. Since iodo-casein is believed to contain about 3 per cent L-thyroxine<sup>4</sup>, this comparison raises the alternative possibilities that these published estimates of the thyroxine content of iodo-casein preparations are in error, or that the efficiency of oral utilization of thyroxine combined in iodo-casein is much lower than that of the pure hormone.

In a previous experiment involving fourteen daily subcutaneous injections of 10 mgm. DL-thyroxine into lactating cows, Folley and White<sup>8</sup> obtained a response at the end of the second week of the injection period amounting to approximately 5 lb. milk/cow/day. From the data in the table, linear interpolation shows that a response of about this magnitude was given by approximately 82 mgm. L-thyroxine administered by mouth. Taking the relative biological activities of L- and DL-thyroxine as very near 2:1<sup>4,7</sup>, it follows that the oral/parenteral ratio for L-thyroxine in the cow is approximately 16:1.

The effects of the treatments on the fat and non-fatty solids (no significant changes), lactose, protein and nitrogen distribution of the milk have been studied by Dr. S. J. Rowland; on certain milk vitamins by Dr. S. Y. Thompson; and on milk iodine by Dr. H. H. Green. These results, together with the changes in milk phosphatase, will be fully reported later.

Since these results seem to open up the possibility of using synthetic L-thyroxine in practice for stimulating milk yield in cattle, an examination of the advantages of the pure hormone over iodo-casein may be of interest. These are: (a) there is no necessity for bioassay, a troublesome and unreliable procedure unavoidable with iodo-casein; (b) the total iodine fed is much less than with a dose of iodo-casein of equal activity and there is no risk of iodism; and (c) L-thyroxine seems to be virtually tasteless and when incorporated into suitable tablets is readily eaten by cows, which is not always the case with iodo-casein.

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