## Dietary Citrate and Hypomagnesæmia in the Ruminant

THE sudden onset of clinical hypomagnesæmia in the lactating cow most commonly occurs soon after the change from stall feeding to grazing fresh spring grass, and in the absence of any marked reduction in intake of magnesium. This condition is probably brought about by reduced absorption of magnesium; but the reasons for this are not fully understood. Marked reductions in output of urinary magnesium on changing the diet from hay or grass nuts to fresh grass have been described for sheep[1] in spite of increased intakes of magnesium; this probably indicates reduced absorption. Care[2] recently calculated that a 50 per cent reduction in absorption could lead to the development of hypomagnesæmia within 7 days in sheep.

Mineral balance of herbage[3], low sodium intakes[4], and increased ruminal ammonia production[5] from the appreciable amounts of soluble nitrogenous constituents of spring herbage have all been suggested as precipitating factors, but none of these has been consistently implicated in clinical cases of the disease. In the course of an investigation into the effects of adding organic acids and their salts to the diet of ruminants, we have obtained evidence that dietary citrate levels may be related to the occurrence of hypomagnesæmia.

Eighteen 4–6 month old Ayrshire heifer calves were housed in individual pens and fed 3·5 lb. of a commercial concentrate, 0·5 lb. crushed barley and hay *ad lib.* to a maximum of 4 lb. daily. The calves were paired and allocated at random to treatments providing (*a*) 30 gm. sodium chloride or (*b*) 50 gm. granular sodium citrate in individual daily doses mixed with the barley. Each supplement provided 11·8 gm. sodium per day.

Intakes of food and gains in live weight were similar for both treatments over an 8-week experimental period. In the eighth week, blood samples for the determination of serum calcium, magnesium and inorganic phosphorus were taken on two occasions with the results shown in Table 1. Those calves which had received sodium citrate showed significantly lower levels of serum magnesium and appreciably lower levels of serum inorganic phosphorus than the calves which had received sodium chloride.

Table 1. EFFECTS OF SODIUM CITRATE UPON SERUM CALCIUM, PHOSPHORUS AND MAGNESIUM (MGM./100 ML. SERUM: MEAN OF TWO OBSERVATIONS PER CALF)

| Treatment | Magnesium | Calcium | Phosphorus |
|---|---|---|---|
| (*a*) Sodium chloride | 2·11 | 9·47 | 9·18 |
| (*b*) Sodium citrate | 1·86 | 9·73 | 8·43 |
| Significant difference ($P = 0·05$) | 0·18 | 0·52 | 0·79 |

The results suggest that the ingestion of small quantities of sodium citrate reduce levels in serum of magnesium and possibly inorganic phosphorus. Since skeletal magnesium is more readily available in the young calf than in the adult cow[6] any factor which interferes with magnesium absorption would be expected to take longer to reduce calf serum magnesium significantly.

The daily intake of citric acid (as sodium citrate) amounted to 1·0 per cent of the dietary dry matter; levels of 0·4–0·7 per cent were reported for fresh perennial ryegrass by Hirst and Ramstad[7]. The occurrence of hypomagnesæmia might thus be associated with increased intakes of citrate from herbage. Further experiments are in progress to extend these observations to the lactating cow and to determine more precisely the effect of citrate intake on magnesium metabolism in the ruminant.

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## Difference in Metabolism of Labelled Thyroxine between Thyrotropic and Adrenotropic Mouse Pituitary Tumours

LITTLE is known about the mechanisms within the pituitary which are involved in the control of thyrotropin secretion exerted by circulating thyroid hormone. In the work reported here mouse pituitary tumours were used to examine this problem since each of these several tumour types reflects quite closely the behaviour of its prototype cell in the normal pituitary. The results suggest there may be a special thyrotropin-secreting cell with an unusual pattern of metabolism for thyroxine. Thus, mouse pituitary thyrotropic tumours were found to contain large amounts of labelled 3,5,3′-triiodothyronine ($T_3$*) 4 hr. after injection intraperitoneally of labelled thyroxine ($T_4$*), whereas mouse pituitary adrenotropic tumours and other tissues contained none.

Three strains of thyrotropic tumours in $LAF_1$ mice, originally made available by Furth[1], were used. Several transplants of an adrenotropic tumour in $LAF_1$ mice also were furnished by Dr. Furth. A spontaneous fibrosarcoma in $LAF_1$ mice; kidney, muscle and pituitary from thyroidectomized $LAF_1$ mice; and a carcinoma of the breast in Swiss mice from Dr. S. Graff were examined as control tissues.

With mouse pituitary tumours, valid conclusions generally may be drawn from groups of 4 mice each (Furth, J., personal communication). Nevertheless, all experiments were repeated for confirmation. Groups of 5 mice each were used for the thyrotropic tumours, and groups of 3 mice each with the other tumours due to a limited number of mice available.

Since two of the three thyrotropic strains grow only in thyroidectomized mice, the thyroid was destroyed in all thyrotropic tumour hosts[2]. The adrenotropic tumours were maintained both in intact and adrenalectomized mice given deoxycortisone subcutaneously once a week.

The biological methods[2] and the methods for extraction of serum[3] used by this laboratory have been detailed elsewhere. Chromatographic separation of the iodinated compounds in tissues was done by the methods of Roche *et al.*[4]. 10–20 μc. $T_4$* (Abbott) repurified, when necessary, by paper chromatography and containing 0·4–1 μgm. stable $T_4$, were injected intraperitoneally and autopsy performed 4 hr. later. All tissue samples were rapidly weighed, counted for radioactivity to 5 per cent accuracy in a well-type scintillation counter and then frozen and lyophilized.

After chromatography, further identification of the radioactive compounds was made by two-dimensional