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Relationship of the thyroid gland and calcium metabolism in the bovine

William Francis Byrne

To the Graduate Council:

I am submitting herewith a dissertation written by William Francis Byrne entitled "Relationship of the thyroid gland and calcium metabolism in the bovine." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Animal Science.

E. W. Swanson, Major Professor

We have read this dissertation and recommend its acceptance:

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To the Graduate Council:

I am submitting herewith a dissertation written by William F. Byrne, entitled "Relationship of the Thyroid Gland and Calcium Metabolism in the Bovine." I recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Animal Science.

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RELATIONSHIP OF THE THYROID GLAND AND CALCIUM METABOLISM IN THE BOVINE

A Dissertation

Presented to

the Graduate Council of

The University of Tennessee

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

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by

William F. Byrne

March 1971

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ABSTRACT

Two groups of experiments were conducted to investigate the relationship of the thyroid gland and calcium metabolism in the bovine.

The first group included investigations of the effects of thyroid status (calcitonin and thyroxine status) on the response of mature cattle and calves to hypercalcemia induced by intravenous infusion of calcium solutions and changes in serum calcium at parturition.

Three unsupplemented athyroid cattle cleared infused calcium from the blood more slowly than three controls. However, five thyroid-damaged cows fed iodinated casein cleared excess calcium from blood as well as five controls. In the third experiment, six thyroid-damaged calves which were receiving slightly excessive thyroxine therapy cleared infused calcium from blood as well as controls. The results of these experiments indicated that thyroxine therapy restored the normal ability to counteract hypercalcemia. No defect logically attributable to calcitonin was evident.

The hypercalcemic response of three thyroid-damaged calves and three controls was tested before and during thyroxine therapy to the thyroid-damaged calves. Unsupplemented thyroid-damaged calves cleared excess calcium from the blood as well as controls. When excessive thyroxine therapy was given to the thyroid-damaged calves their ability to counteract hypercalcemia appeared to be decreased. This was attributed to increased bone calcium turnover stimulated by excess thyroxine in the supplemented calves. Two hyperthyroid control calves cleared calcium from blood at a slower rate than two thyroid-damaged calves.

Effects of excess thyroxine on bone calcium turnover could have been responsible for this occurrence. No consistent effects of thyroid status on serum phosphorus and magnesium were noted in these tests. The results did not demonstrate a major role for calcitonin in the hypercalcemic response of calves. Important effects of thyroxine could be inferred from the data.

Blood samples were taken before calving, at calving, and after calving in six pairs of control and thyroid-damaged cows. A significant drop in serum calcium at calving was noted in controls but not in thyroid-damaged cows. This finding was attributed to release of calcitonin at parturition in the control cows. Hypocalcemic activity was present in the serum of a normal parturient cow, as judged by the decreased serum calcium in normal calves infused with such serum, but no such activity was present in the serum from a thyroid-damaged parturient cow. Calcitonin appeared to be involved in the serum calcium changes at parturition.

In the second group, comprising six experiments, the effects of thyroid status on normal calcium metabolism in cows and calves were studied. In three experiments concurrent 5-day chemical and radiocalcium balances were conducted on calves dosed simultaneously with ^{47}Ca intravenously and ^{45}Ca orally. Bone uptake and gut retention were determined. Lower calcium absorption in three thyroid-damaged calves compared to three controls was indicated in one experiment. Low calcium absorption due, perhaps, to hyperthyroidism in two controls in another experiment could have masked decreased calcium absorption in two thyroid-damaged calves. When excessive thyroxine therapy was given to three thyroid-damaged calves no difference from

absorption by three controls was noted. The results indicated that increasing the level of circulating thyroxine increased the turnover rate of body calcium.

In two experiments a total of five lactating cows were dosed intravenously with radiocalcium to study the effects of thyroxine status on calcium metabolism in lactation. In both experiments increased circulating thyroxine levels, whether induced by injection of thyrotrophin or by direct thyroxine injections, increased the mobilization of body calcium reserves.

The transfer of calcium from dam to fetus in three control and three thyroid-damaged cows was not affected by thyroid status.

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CHAPTER I

INTRODUCTION

The role of the thyroid in the regulation of body metabolism has been established. Thyroxine and tri-iodothyronine control the rate at which substrates are used to produce the high energy compounds required in life processes. Thyroidectomy or hypothyrodism results in decreased productivity and activity accompanied by fattening, abnormal growth, and skeletal abnormalities in young animals. Hormones from the thyroid directly affect calcium metabolism. Thyroxine keeps target cells responsive to the action of parathormone and calcitonin. Calcitonin, produced in mammals by a separate population of thyroid cells, is released into the circulation and regulates the calcium concentration of the extracellular fluid by inhibiting the resorption of bone calcium. The essential role of calcium in many body processes is well established. Therefore, finely balanced hormonal control of its metabolism would be expected.

Thyroid-calcium relationships in dairy cattle have not received the attention they deserve. Sale of milk from dairy cows is the greatest single source of farm income. Apart from this economic consideration, nutritional and physiological aspects of dairy cattle husbandry indicate a study of these relationships would be rewarding. Dairy cattle normally consume diets in which the ratio of calcium to phosphorus is large. However, the range of calcium to phosphorus ratios which cattle can tolerate is remarkable. In contrast, monogastric animals do not tolerate substantial changes from a ratio of one.

Large amounts of calcium and phosphorus are required for normal skeletal development in the growing calf. After weaning, these requirements must be satisfied from diets that have large calcium to phosphorus ratios and which contain substances that decrease the availability of calcium and phosphorus. Study of the effects of thyroid hormones on the gut and developing skeleton of calves could lead to an understanding of the mechanism by which the development of a functional rumen effects changes in calcium metabolism regulation. Mature dairy cows, especially older cows, are frequently afflicted at parturition with a serious metabolic disturbance of calcium metabolism, milk fever. The condition is more prevalent in some breeds than in others, It is characterized by low serum calcium and, in many cases, phosphorus. Many investigators feel that this condition is either under hormonal control or due to endocrine malfunctions of unknown nature. Since the thyroid is known to secrete a hypocalcemic hormone, the relation of the thyroid to milk fever is an obvious area for fruitful study. After parturition, high producing dairy cows are unable to ingest and absorb sufficient calcium to satisfy the requirements for high milk production. Consequently large amounts of body stores must be mobilized in early lactation and replaced in late lactation or during the dry period. The role of thyroid hormones in the tremendous calcium and phosphorus exchanges during lactation certainly deserves study.

The danger of radioiodine thyroid damage in cows exposed to fallout from nuclear "events" whether accidental or intentional, can not be overlooked. With respect to calcium metabolism, complete or partial destruction of the thyroid would impair the ability to counteract hypercalcemia. However, the normal tendency is toward hypocalcemia due

to skeletal uptake. Thus the more serious consequence of thyroid damage may be loss of thyroxine with resulting insensitivity of the resorbing bone surfaces to parathormone. Decreased influx of calcium and phosphorus from the gut as a result of decreased feed intake would aggravate the situation. These speculations deserve experimental investigation.

CHAPTER II

REVIEW OF LITERATURE

A. Current Concepts of Calcium Regulation

This section presents many of the significant findings pertaining to the development of the current concept of regulation of calcium metabolism. Recent reviews on this subject have been published (38, 46, 78, 163).

Parathyroid hormone. The parathyroids are small glands of ultimobranchial origin (38). Removal of parathyroids caused tetany which was associated with low serum calcium (170). Collip (32) demonstrated that extracts of parathyroids produced hypercalcemia when injected into dogs. The pure hormone was isolated in 1959 by Aurbach (9).

Parathyroid secretion is decreased by hypercalcemia (23) and increased by low calcium diets (156) and low serum calcium concentrations (38). Copp (38) reported that McLean concluded parathyroid function was decreased in hypercalcemia and increased in hypocalcemia. Potts and associates (143) concluded that parathormone secretion was dependent on serum calcium and showed that the plasma parathormone concentration was linearly and inversely related to serum calcium.

Potts et al. (143) also showed that in vivo, the half-life of parathormone in cows and rats was only 10 to 25 minutes. However, Rasmusson et al. (147) found that injection of 0.2 mg of pure bovine parathormone into rats resulted in a rise in plasma calcium which lasted for 30 hours. Administration of actinomycin D, which blocks net RNA synthesis, prior

to parathormone injection suppressed hypercalcemic activity after six hours. These observations have been confirmed in tissue culture studies (38). This RNA dependent phase of parathormone action has been attributed to vitamin D action on subcellular processes (46) but the mechanism remains unknown (37).

The major site of parathormone action is in bone (37) where it mobilizes calcium from compact bone of rats (10, 52). Parathormone also affects the transfer of calcium across the gut wall of the dog (44), increases filtration and decreases resorption of phosphorus in the kidney (170), and promotes increased resorption of calcium in the kidney tubule (38).

Calcitonin. Copp and associates (39, 40) first proposed the existence of calcitonin on the basis of their perfusion studies with dogs. They proposed a parathyroid origin for the hormone, but the parathyroid origin of calcitonin could not be confirmed. Later work (77) with rats indicated that a hypocalcemic principle was released from the thyroid. This observation was confirmed by the results of perfusion studies in goats (56) and results of experiments in which thyroid extracts were injected into goats (56) and rats (79). These experiments and those of Care and others (29) with pigs demonstrated that the parathyroid was not necessary for hypocalcemic activity. Talmage and associates (166) reported a series of experiments which demonstrated that in rats loss of the thyroid impaired the response to hypercalcemia. Hypocalcemic activity of human thyroids has also been demonstrated (6).

Calcitonin does not come from the acinar cells in the thyroid but from the parafollicular or 'C' cells entrapped there during fetal

development (22, 38). The 'C' cells are identical to those found in the ultimobranchial body which in birds, fish and reptiles contains large amounts of calcitonin (38, 41).

The primary function of calcitonin is to lower calcium concentration in the extracellular fluid (6, 29, 39, 40, 56, 77, 79) which effect is accomplished by direct inhibition of bone resorption. English workers (107) showed that calcitonin treatment of rats decreased hydroxyproline excretion which indicated decreased collagen breakdown. Work at other laboratories with rats (82,90, 160) has shown that calcitonin treatment resulted in decreased loss of radioactivity from prelabeled bones. These results have been confirmed *in vitro* (4, 58, 144, 145). Calcitonin is effective in the absence of the kidney (5, 150) and the gastrointestinal tract (45, 87) in the rat. The hypocalcemic action of calcitonin is dependent on the amount of bone resorption. Care and Duncan (28) demonstrated that decreased response to calcitonin in old sheep was due to decreased bone responsiveness. Also, recent reports (133, 150, 165) have shown that the phosphaturic effects of calcitonin reported by many workers (38) were due to stimulation of parathormone secretion by induced hypocalcemia.

Care *et al.* (27) measured calcitonin secretion rate in pigs and found it to be a simple linear function of serum calcium concentration. The pituitary was not necessary for response (26). Klein and Talmage (90) and others (61) demonstrated calcitonin secretion at normal serum calcium levels in the rat. Calcitonin is cleared rapidly from the blood of rabbits (94) and pigs (175) and some component of blood rapidly inactivates calcitonin (167).

Vitamin D. The literature on vitamin D has been reviewed by DeLuca (46). He concluded that the primary action of the vitamin was to increase the intestinal absorption of calcium and secondarily phosphorus. This increased absorption was shown to be dependent on DNA directed protein synthesis. Vitamin D increased tubular resorption of calcium in the kidney. Mobilization of bone calcium in response to physiological doses has been noted in the rat (47). This effect was dependent on DNA directed protein synthesis. Parathormone mobilization of bone calcium depended upon the presence of vitamin D (46, 69, 121). Some workers (47) stated that impaired response to parathyroid hormone after actinomycin-D injection in rats (147) was due to inhibition of vitamin D initiated DNA dependent protein synthesis. Norman and associates (129) reported that vitamin D was metabolized to a more active form which associated specifically with a receptor site on DNA. The net effect of vitamin D is to increase the ion product of calcium and phosphate in the extracellular fluid so that proper bone mineralization can occur (46). Neither absence (121) nor excess (113) of vitamin D impaired the hypocalcemic action of calcitonin in the rat.

DeLuca et al. (47) have proposed that the mobilization of calcium in bone cells is due to intracellular action of vitamin D. Parathormone and calcitonin regulate release of the intracellular calcium from bone cells by increasing or decreasing bone cell membrane permeability to calcium. This interesting hypothesis can explain all of the known relationships concerning the interactions of these three factors on bone calcium regulation.

B. Involvement of Thyroxine in Calcium Metabolism

Clinical evidence. According to Gittes and Irvin (60) Aub reported that hypothyroid patients showed higher net absorption of calcium than controls. Jowsey and Detenbeck (83) reported that Lowe and associates found prolonged hypercalcemia following oral calcium loading in hypothyroid patients as compared to controls. Thyroxine therapy of one case returned the response to normal. The effect was also seen in ^{131}I thyroid-damaged rats. Krane and associates (91) studied hypothyroid, hyperthyroid, and normal individuals injected intravenously with radiocalcium. Hypothyroid patients had slower declines of serum specific activity than normal. Hyperthyroid patients showed more rapid clearance of radiocalcium than normal. After five months of thyroxine treatment, hypothyroid patients showed normal response. They concluded that thyroid status affected the turnover of body calcium by affecting the rate of bone formation and resorption. Adams and associates (2) studied twenty-two patients with hypothyroidism. Infusion of EDTA caused a greater decrease in serum calcium and a significantly slower recovery in hypothyroid patients than controls. This finding indicated bone mobilization was being impaired. Treatment of five patients with thyroxine returned the response to normal. Goldsmith et al. (83) also noted impaired ability to counteract hypocalcemia induced by EDTA infusion in untreated hypothyroid patients as compared to thyroxine treated patients and suggested that bone mobilization was the cause. Riggs, Jones, and Arnaud (148) studied the hypercalcemic response of nine normal and eight hypothyroid persons. Blood clearance of intravenous calcium was significantly slower for the hypothyroid patients than controls. Thyroxine therapy reduced, but did not eliminate,

the difference. Treatment of hypothyroid children with thyroxine (81) restored normal bone development by decreasing both resorption and accretion.

Experimental evidence. Gittes and Irvin (60) studied the effects of parathyroidectomy and thyroparathyroidectomy on the ability of rats to counteract hypercalcemia subsequent to intraperitoneal inection of calcium. Thyroxine replacement therapy abolished differences in resting serum calcium values between the groups. Thyroxine therapy restored the ability to counteract hypercalcemia to about 50% of the control levels. They concluded that thyroxine was required for the normal hypercalcemic response. Similarily, Morii and Talmage (122) found that rats with ^{131}I damaged thyroids or on iodine deficient diets were unable to reduce hypercalcemia as well as controls. Pre-treatment of rats subjected to parathormone overdosage with thyroxine (59) abolished the response to parathormone. Thyroxine appeared to increase the turnover of circulating calcium. Massive doses of dinitrophenol did not affect parathormone action. The conclusion was that the effects of thyroxine on parathyroid action were specific rather than general. Green and associates (62) studied the effects of tri-iodothyronine injections on calcium kinetics in thyroparathyroidectomized dogs. Both accretion rates and exchangeable pool size were increased after injection.

The effect of altered thyroid status on the calcitonin content of rat thyroids was studied by Yasumura et al. (176). Hyperthyroidism caused a significant 27 to 30% decrease in thyroidal calcitonin content. This was attributed to increased bone resorption stimulated by thyroxine. Italian workers (7) studied calcium metabolism in rats with severe

thyroid damage. They found that both accretion and resorption of bone were decreased in thyroid-damaged rats compared to controls. The metabolism of collagen in hypo- and hyperthyroid rats was studied by Kivirikka and associates (89). Collagen was labeled by injecting ^{14}C-proline 30 days prior to test. Thyroxine injections increased the urinary excretion of ^{14}C-hydroxyproline indicating bone resorption. Hypothyroid rats incorporated significantly less proline and turnover was slower. Khoo and Kowalewski (88) reported that bones from hypothyroid rats lost significantly more calcium in vitro than controls. Thyroxine treatment resulted in a significantly smaller loss in vitro than controls. These authors cited work by Lengemann which indicated that thyroxine treatment inhibited the release of radiocalcium from bones and that bones from hypothyroid rats liberated significantly more calcium than bones from controls.

Freedland and associates (57) reported that hyperthyroidism in rats promoted the net excretion of calcium across the gut wall. Extended hyperthyroidism resulted in reduced bone formation compared to controls. Noble and Matty (128) confirmed these findings in studies with everted gut sacs from rats given daily thyroxine injections. The active transport of calcium was almost completely inhibited. Levin (99) concluded that thyroidectomy also decreased absorption and motility in the small intestine of the rat.

Burkhart and Jowsey (21) studied the effects of thyroidectomy, parathyroidectomy, or thyroparathyroidectomy on the osteoperosis caused by limb disuse in adult dogs. Thyroidectomized dogs received no supplementation. Thyroidectomy was as effective as parathyroidectomy in inhibiting bone formation or resorption. Thyroparathyroidectomy was no more effective than thyroidectomy. Parathyroidectomy was followed by a rise

in bone formation but thyroidectomy abolished the increase. Thyroxine appeared to be required to keep bone responsive to parathormone.

Jowesy and Simons (84) found that thyroidectomy completely abolished the hypercalcemia subsequent to adrenalectomy. Three groups of dogs were subjected to adrenalectomy 12 to 207 days after either thyroidectomy, parathyroidectomy, or thyroparathyroidectomy. Parathyroidectomized dogs showed a rise in serum calcium to greater than 17 mg per 100 ml (mg/100 ml) of serum. Thyroidectomized dogs showed no rise and, thyroparathyroidectomized animals were intermediate. Administration of thyroxine to two of the thyroidectomized dogs resulted in rapid and sustained rise in serum calcium within three days. Their conclusion was that thyroxine affected bone responsiveness. The unusual finding of increased bone resorption after parathyroidectomy was not explained.

In another report (3) the effect of thyroxine induced hyperthyroidism on calcium metabolism was studied using intact and parathyroidectomized dogs. In both groups hyperthyroidism caused an increase in bone resorption and accretion. Resorption occurred before and to a greater extent than accretion. The hypercalcemia observed was attributed to increased bone resorption. Bone resorption in parathyroidectomized dogs was increased 300% over pre-experimental values. Intact animals responded to hyperthyroidism with greater bone formation than parathyroidectomized animals. These findings indicated that bone resorption occurred in the absence of parathormone and that thyroxine had direct effects on bone independent of parathyroid status.

A very thorough study was recently reported by Jowsey and Detenbeck (83) in which the response of dogs to EDTA infusion, calcium loading, parathormone injection, and calcitonin injection was determined in the

normal, thyroidectomized, euthyroid (adequate thyroxine therapy to thyroidectomized animals), and hyperthyroid (excessive thyroxine therapy) state. Thyroidectomy resulted in a significantly slower response than normal to EDTA or calcium infusion. Adequate thyroxine therapy returned the response to normal but excessive thyroxine did not increase response. Serum calcium response to parathormone was decreased after thyroidectomy. Adequate thyroxine increased response to normal and excessive thyroxine increased response above normal. Thyroidectomy destroyed the normal response to calcitonin. Treatment with adequate thyroxine restored the response to normal. Excessive levels did not increase response above control. They concluded that thyroxine had direct effects on bone cells by influencing bone accretion and resorption.

The evidence presented indicates that thyroxine has a direct and important role in the regulation of calcium metabolism. Any meaningful study of thyroid-calcium relationships should include estimates of the effects of both calcitonin and the iodinated thyroid hormone.

C. Calcium Metabolism and Regulation in Cattle

Absorption. Calcium is absorbed primarily from the abomasum and small intestine of cattle (31, 42). According to Beaumont and associates (11) losses of calcium to the digestive tract, endogenous secretion, were first reported by Voit. This finding has been confirmed by others (33, 112, 132, 134). Hansard and associates (66) showed that 19% of the fecal calcium of mature cattle in positive calcium balance was of body rather than dietary origin. These workers also reported that the utilization of dietary calcium decreased with age (67). These findings have been confirmed in sheep (126) as well as cattle (54, 66).

Absorption appeared to depend upon the needs of the animal (17, 18, 19, 35, 36, 71, 134). However, large negative calcium balances of lactating cows (49, 50, 112, 132) indicated that increased absorption could not satisfy all requirements for high milk production.

Utilization of dietary calcium in cattle has been reported to depend on the ratio of calcium to phosphorus in the feed (17). However, the percentage of calcium in the diet also has been shown to affect absorption (103). Small amounts of grain added to all roughage rations increased availability of calcium and phosphorus (71). Also, calcium in diets of low pH appeared to be utilized more efficiently than calcium in diets of high pH (70, 130) even when the amounts of calcium and phosphorus were the same in both diets (130). Low availability of calcium from hay noted by some workers (68) was attributed to the presence of calcium binding factors in hays and to increased endogenous losses. The role of calcium binding factors has been questioned (17) since such complexing agents appeared to be metabolized in the rumen. However, calcium-phytate-phosphorus complexes appeared to be stable and relatively insoluble (168). Van't Klooster (171) found that the majority of calcium in feces and ingesta was in an unavailable bound form. High roughage rations increased the amount of bound calcium in both feces and ingesta. Replacing roughages with cereals resulted in increased calcium digestibility and more positive balance (134) even when calcium intake decreased.

Body storage and mobilization. Radioactive calcium leaves the blood rapidly, equilibrates rapidly with soft tissues, and is deposited mainly in the skeleton. Approximately 85% of the radiocalcium which entered the blood was retained in the body (65, 66). Exchangeability of skeletal

calcium decreased with age (65). This could partially explain the finding that old cows could not counteract hypocalcemia as well as young cows (123). However, old cows responded to hypercalcemia as well as young cows (1). Cattle showed the normal responses to parathormone stimulation (108, 146). A large portion of the calcium required for milk production in early lactation must be supplied from body stores (49, 50, 112).

The transfer of calcium from dam to fetus was studied by Plumlee and associates (141). They concluded that calcium could move rather freely across the placenta. However, Payne and coworkers (137) showed that radiocalcium injected directly into the fetus could be quantitively recovered from the uterus and its contents 24 hours later. Symonds et al. (162) reported that the transfer rate of calcium to the fetus during the last 10 days of gestation was 5.3 g per day. Hansard (64) studied the transfer of radiocalcium from dam to fetus at 270 days of gestation in heifers. Only 22.4% of the radiocalcium which entered the blood was recovered in the products of conception. The fetus contained 95% of all activity in the conceptus.

Milk secretion. Calcium requirements for milk production are high. Reported losses of calcium in the colostrum at calving ranged from 7 to 25 g per day (76, 130, 137, 162). Colostrum loss increases with age (137). The increased need for calcium came at the time when ability to mobilize body reserves was below normal (135). Decreased appetite at parturition (119, 120) could aggravate the situation. The fall in serum calcium reported at parturition (16, 17, 72, 86, 110, 137) increased in severity with age (137) and appeared to depend on diet (17, 86). Mastectomy prevented 80% of the usual serum calcium drop at parturition (127).

The mammary accumulation of calcium in lactation increased two to eight fold over that in the dry period (153). Removal of calcium from blood at a rate comparable to mammary uptake resulted in increased circulating parathormone levels and calcium mobilization (146).

Mammary uptake of calcium in lactation ranged from 0.14 to 0.70 mg per 100 ml of blood which passed through the udder (130, 153). Normal milk contained 110 to 120 mg per 100 g or 1.2 g per kg (130). Other authors (111) placed the concentration at 2.2 g per kg. Content of calcium was slightly higher in colostrum (76, 130). Calcium of milk was derived from the calcium of blood (8, 53, 96, 172) ostensibly the ultrafilterable fraction (85). The time required for calcium to pass through the secretory epithelium into milk was 3 to 5 hours (8, 53, 85, 96, 173). However results from studies utilizing radiocalcium showed that calcium was stored in the mammary glands (173) and, that this pool of calcium was participating in the secretion of calcium into milk (161).

Role of gut in calcium regulation. After birth, all calcium which enters the body normally must pass the gut wall. Cragle and associates (42) studied the net absorption of calcium throughout the digestive tracts of 30 cattle of various ages. Net absorption did not occur from the rumen. Absorption was high from the abomasum and first part of the small intestine. Little net absorption occurred thereafter. Chandler and others (31) found that 20.8% of a dose of ^{45}Ca placed in the abomasum was absorbed within 25 minutes after dosing. Hansard, Comar, and Plumlee (66) found significant quantities of intravenously administered radiocalcium in all sections of the digestive tract except the large

intestine, within 10 minutes after administration. Thus, endogenous secretion occurred in sections where net absorption had been shown to occur. Large amounts of calcium were recycled via the saliva.

Hansard et al. (67) studied the utilization of calcium in cattle ranging in age from 10 days to 190 months. Absorption, true digestibility, and retention of calcium decreased with age. In young calves 98% of the dietary calcium was absorbed. Nearly all fecal calcium was of body origin. Endogenous loss of calcium increased with age. At maturity, excretion of calcium exceeded the dietary intake. This resulted in a -3% apparent digestibility. Losses of calcium were very large in older cattle resulting in a -28% apparent digestibility. Corresponding true digestibilities were 36 and 32% for the mature and old cattle respectively. The apparent calcium absorption from a diet high in calcium was reported to be higher for young cattle than older ones, 537 vs 341 mg per $kg^{0.60}$ per day (54). Younger cattle adjusted their absorption to the high calcium diet more quickly than older ones. Conrad and Hansard (34) found the true digestibility of calcium from a hay-grain diet to be 47.7% in growing steers and endogenous losses to be 2.27 g per day. In nonlactating cows (35) the true digestibility of calcium of a similar diet was 33.1% and the endogenous loss was 11.3 g per day. Hansard, Crowder and Lyke (68) found the true digestibility of the same ration was 60% in young steers but decreased to approximately 40% in mature steers. Daily endogenous loss was also higher in older animals. If endogenous loss was expressed per kg of body weight, the loss was approximately constant over all age groups averaging about 16 mg per kg (67, 68).

Boda and Cole (17) concluded that cattle responded to prolonged calcium deficiency by decreasing endogenous losses and increasing intestinal absorption. Luick, Boda, and Kleiber (103) found that feeding rations of low calcium content but adequate in phosphorus resulted in increased calcium absorption and decreased calcium loss. Lengemann (95) fed paired calves either a high calcium or low calcium diet for 6 months. Then he determined the endogenous loss and true digestibility of dietary calcium. There was no difference between animals raised on the two rations. In a study reported by Converse (36) heifers were raised from 6 months on a diet containing 0.29% calcium. The animals were maintained on the diet throughout their productive life. There was no difference in growth or milk production of these animals compared to controls fed higher levels of calcium. In another trial a diet of 0.16% calcium content proved adequate for growth and production. The ability of these animals to satisfy calcium requirements indicated that absorption had increased. Paquay and associates (134) fed a total of 55 different rations to 127 dry and 35 lactating cows and measured calcium balance and digestibility. They concluded that ration composition was the most limiting factor concerning absorption of calcium. If cereal grains replaced part of the dietary roughage, calcium absorption was sufficiently increased to meet the requirements for milk production of 20 kg per day.

Visek, Barnes, and Loosli (172) gave two goats oral doses of ^{45}Ca in early, middle, and late lactation. They noted that the percentage of the dose which appeared in the blood decreased as lactation advanced. Fecal excretion of radiocalcium increased with advancing lactation. They concluded that absorption was being regulated by the needs of the animal. Boda and Cole (17) concluded that the greatest absorption and utilization

of dietary calcium occurred in peak lactation. Reports from the Vermont station (49, 50) noted that the fecal loss of calcium increased as lactation progressed. A Belgian report (134) showed a highly significant negative relationship, independent of dietary calcium intake, between milk calcium loss and fecal calcium loss. Conrad and associates (35) found that the true digestibility of dietary calcium was increased from 33.1% in dry cows to 44.3% in lactating cows. A report by Hibbs and Conrad (71) showed that highest net absorption accompanied the highest milk production.

Lactating ewes (18) absorbed more of their dietary calcium than dry ewes. A maximal net absorption of 28% of the calcium intake was observed. Other English work with cows (152) showed that dry and parturient cows absorbed as much oral radiocalcium as cows in peak lactation. Muir and associates (124) found that variations in feed intake accounted in part for variations in response to hypocalcemia. This observation could mean that calcium in the gut is part of the available body stores. Others (108) reported that parathyroidectomy of cattle was followed by hypocalcemia due to decreased absorption.

In old cows a fast of 48 hours was accompanied by a fall in serum calcium to 4.5 to 6.0 mg/100 ml of serum and symptoms of milk fever (130). Robertson and associates (149) confirmed this finding. Moodie induced bowel stasis in cattle (117) and sheep (118). In two lactating cows there was distinct hypocalcemia. Within 16 hours serum calcium had dropped to 5 mg/100 ml. In three young cows there was no effect on serum calcium. In the sheep hypocalcemia was less pronounced and inconsistent. Payne (136) also reported hypocalcemia due to decreased gut motility. Moodie and Robertson (119) reported that appetite, and consequently,

intake of calcium were depressed about 30% prior to parturition. The decrease was greatest in older animals. Blood calcium level was directly related to feed intake. These authors reported (120) that bowel stasis was not required for the observed depression of feed intake at parturition.

Role of the skeleton in calcium regulation. Ellenberger and associates (51) analyzed the bodies of 130 dairy animals of various ages. They found that 98.2% of all the calcium in the body was in the skeleton. Hansard and coworkers (67) found that radiocalcium which entered the blood was retained largely in the skeleton. About 100 times more radiocalcium was found in bones than in any soft tissue. However, the specific activity of bone calcium was lower than soft tissue which meant that much of the calcium in bone was not exchangeable. In later work (65) Hansard concluded that the skeletal uptake of calcium from the blood was less in older animals than in younger animals. As a result the soft tissue uptake of calcium increased with age. Clearance of radiocalcium from blood was three times faster in young animals than older animals. Comparison of the specific activity of blood to that of spongy and compact bone, gave the maximum and minimum percentage of bone calcium which was available for exchange. These limits decreased with age from 60 and 9% at 6 months to 5 and 2% at 60 months. Luick and associates (102) found that low calcium diets increased the amount of exchangeable body calcium in old cows from 37 to 60% of the total body calcium. Bone calcium turnover was increased.

The ability of cows to mobilize body calcium reserves in response to hypocalcemia was studied by Muir, Hibbs, and Conrad (123). Older

cows showed decreased ability to counteract hypocalcemia induced by EDTA infusion. Variations in the level of hydroxyproline excreted in the urine accounted, in part, for variation in the response of cows to EDTA infusions (124). Payne (135) studied the ability of cows in different physiological states to mobilize body reserves in response to induced hypocalcemia. He found that cows in late pregnancy had smaller mobilizable reserves, 6.4 g, than dry or lactating cows, 7.67 or 7.18 g respectively. Heifers had smaller mobilizable reserves, 5.8 g, than the older cows. The mobilization rate of cows in late pregnancy was only 0.5 g per hour. Values for dry and lactating cows were 0.7 to 0.8 g per hour. Heifers mobilized their reserves as quickly as old cows.

In lactating ewes (18) bone resorption was high in early lactation, 646 mg per kg per day, and decreased in proportion to milk yield to 6 mg per kg per day in late lactation. Payne's results (135) did not indicate the same was true in cattle. Other workers (14) reported that both blood and urinary citrate were increased at parturition and that this finding indicated increased bone resorption. Cows which subsequently developed milk fever were in negative calcium balance at parturition (174). Hibbs and others (73) found serum alkaline phosphatase to be decreased at parturition. Nurimo (130) could not demonstrate an increase in bone resorption, as measured by the ratio of urinary hydroxyproline to creatinine, in cows at parturition. Mayer and associates (110) found normal or increased levels of parathormone in parturient cattle. The level was inversely related to serum calcium. Other work from this group (146) showed that cattle responded to hypocalcemia with increased bone resorption. However, Sansom (152) could not demonstrate increased bone resorption in parturient cows or cows at peak lactation. The rate

of bone calcium accretion was decreased from 22.3 to 17.6 g per day within 2 weeks after calving.

The large negative calcium balances in early lactation indicated that net mobilization of body stores was occurring. Meigs (112) reviewed the early work and concluded that utilization of body stores in early lactation was large in high producers. The studies of Ellenberger, Newlander, and Jones (49, 50) showed that the cumulative loss of calcium from body stores during the first 35 weeks of lactation in 10 cows ranged from 16 to 32 kg. Body reserves were rapidly replenished later and cows stored from 273 to 1380 g of calcium per lactation. Cattle raised and maintained on low calcium diets (36) secreted a greater percentage of their total calcium intake in milk than normals, which response could have been due to smaller body reserves as a result of the low calcium rearing diets.

Role of kidney in calcium regulation. Most investigators have found that loss of calcium through the urine is unimportant in cattle (35, 66, 102, 108, 134, 169, 172). In certain circumstances the urinary loss of calcium was increased. Blaxter (13) noted an increased loss of calcium in the urine of sheep fed thyroprotein. Hart and associates (70) noted that feeding small amounts of strong acids to cows resulted in a large increase in urinary calcium excretion. Urinary loss of calcium at parturition was increased 30 times in cows developing milk fever (15). Administration of parathormone to thyroparathyroidectomized cows increased urinary excretion (169). Some workers (65, 172) reported greater urinary excretion of radiocalcium following intravenous administration than following oral administration. Albright and Blosser (1)

found that within 24 hours urinary excretion of intravenously administered 32.7% or 25.5% calcium borogluconate solution averaged 22.4 and 12.5% of the injected calcium respectively, in normal cows. The actual quantities were 3.3 and 1.4 g calcium. The reason for the large loss was attributed to failure of the kidney tubules to resorb all of the calcium filtered from the blood (130).

Role of parathyroid in calcium regulation. Parathyroidectomy of young sheep and cattle has been reported to be fatal (126, 157). Young goats were not similarly affected unless low calcium diets were fed (126, 137). Mature animals withstood the operation well (108, 109, 126, 137, 158, 169).

Todd and associates (169) found that parathyroid extract given subcutaneously to parathyroidectomized cows did not affect milk production or increase calcium absorption from the gut. There was an increase in serum calcium due to mobilization of body stores. The calcium content of milk was not affected. This observation was confirmed by others (140). Todd (169) stated that the endogenous loss of calcium was increased by parathyroid extract. Pennsylvania work (108) showed that parathyroid extract administered to parathyroidectomized cows increased serum calcium levels, bone resorption, fecal endogenous and total fecal calcium, and decreased absorption. However, Luick and others (103) suggested that the increased absorption they noted on low calcium diets could have been due to increased parathyroid activity. Nelson and associates (126) reported that young thyroparathyroidectomized sheep dying in tetany were in positive calcium balance. Payne and others (137) found that absorption, accretion rate, and exchangeable pool size were decreased in

thyroparathyroidectomized goats but endogenous loss was unaffected.

Robinson and associates (151) reported that injections of crude parathyroid extracts into normal calves increased the serum calcium to 18 mg/100 ml. Lotz, Talmage, and Comar (101) could not demonstrate bone calcium resorption in sheep in response to parathyroid extract. An Ohio report (75) showed that injections of parathyroid extract into normal cows caused an increase in serum calcium of 1.5 to 2.0 mg/100 ml. Jackson and others (80) confirmed these observations. Ramberg and associates (146) found that continuous intravenous infusion of EDTA to produce hypocalcemia resulted in increased circulating parathormone levels within 15 minutes. Parathormone levels were inversely related to serum calcium levels. Cows responded to hypocalcemia with increased mobilization of body calcium stores. Luick et al. (102) concluded that feeding low calcium diets stimulated parathyroid function which resulted in increased bone calcium mobility. Capen and coworkers (23) found that hypercalcemia, induced by feeding vitamin D, caused decreased parathyroid activity.

Mayer et al. (110) reported that circulating parathormone levels were normal or above at parturition. Marshank and Jonssen (130) could not find any histological defects in parathyroids from parturient cows. Stott and Smith (159) concluded that the parathyroid was in an active state shortly before parturition but parathyroid activity was decreased during heavy lactation. The failure of some workers (135, 152) to demonstrate increased bone resorption during lactation supports this conclusion. However, the obvious utilization of body stores in lactation (49, 50, 112, 134) indicated that other factors may regulate bone calcium utilization.

Role of the thyroid in calcium regulation. Brewer and associates (20) have recently isolated pure bovine calcitonin from thyroid glands. English workers (139) attempted to measure the calcitonin secretion rate of calf thyroids perfused in vivo with hypercalcemic blood. They were unable to elicit a hypocalcemic response in two 4-week-old calves even with perfusate calcium concentrations of 26 mg/100 ml. In contrast, lambs responded with secretion rates of 700 μ units of calcitonin per minute per kg body weight. Secretion rates of two other calves were only 100-200 μ units per minute per kg body weight. Calves showed a hypocalcemic response to injection of porcine calcitonin. Another report from the same laboratory (98) stated that radioimmunoassayable calcitonin in cattle blood was only about 13 μ units per ml plasma. Values for pigs were more than 1000 times as high. Lavror and Barlet (93) reported that the infusion of 150 mu porcine calcitonin per kg body weight in the calf did not induce a change in serum calcium. Infusion of 63 mu of calcitonin per kg body weight in the cow resulted in a decrease of 20% in serum calcium. Phillippo and associates (139) found that from 80 to 540 mu of calcitonin were required to cause a decrease in serum calcium in calves.

Capen and Young (24) reported that thyroid glands from normally calving cows contained four times as much hypocalcemic activity as glands from cows with milk fever. Histologically, the parafollicular cells of thyroids from cows with milk fever were less numerous and appeared to have discharged their secretory product. Lequin and others (98) reported that calcitonin concentrations in the plasma of a cow with milk fever were increased almost 300%. They also stated that French workers had observed increased calcitonin in cows with milk fever. The

findings of some workers (1, 43) that there was no difference in the disappearance rate of intravenously injected calcium in normal and milk fever cows indicates that the increased calcitonin levels reported by Lequin et al. (98) may not have been affecting calcium metabolism in parturient cows.

Workers at Purdue (131) collected blood from five nonlactating, five parturient, and five lactating cows and infused 1200 ml of plasma from each cow in each group into one of five recipient yearling heifers. The serum calcium response of heifers was followed over the subsequent 72 hours. Plasma from parturient cows caused a sustained decrease in serum calcium. Plasma from other groups had no effect. They concluded that a hypocalcemic principle was present in the blood of parturient cows. Nurimo (130) took blood from 12 parturient cows, nine of which had milk fever, and infused serum into calves. No significant decrease in plasma calcium of the recipients occurred. He stated that calcitonin was not responsible for the drop in serum calcium at parturition.

Capen and Young (25) found that parafollicular cells of cattle thyroids responded to hypercalcemia produced by feeding massive doses of vitamin D. Continued treatment resulted in hyperplasia. Calcitonin content of thyroids from cows so treated was very low. A New York report (92) indicated that the high incidence, 30%, of parafollicular cell tumors in thyroids of bulls was attributable to long periods of excessive calcium intake. They reported that such tumors were accompanied by increased bone mineralization.

Owen (132) studied the effects of thyroxine on calcium metabolism in lactating cows. Injections of 10 mg of thyroxine daily for 28 days did not affect milk calcium or loss of calcium in urine. There was a

tendency for apparent digestibility of calcium to decrease over the injection period. There was a definite increase in fecal loss which was interpreted to mean increased endogenous loss. There was an increased loss of calcium through increased milk yield. After thyroxine was discontinued, there was an improvement in calcium balance attributable to decreased milk production. Blaxter (13) studied the effects of feeding iodinated casein on calcium metabolism in sheep. Feeding 4 to 12 g iodinated casein daily for 24 days was accompanied by a severe decrease in calcium balance, an increase in the urinary excretion of calcium, and a large increase in fecal calcium loss. There was an indication that endogenous calcium losses also were increased. Serum calcium was within the normal range throughout the trial suggesting increased bone turnover. He referred to work by Folley and White which showed thyroxine administration increased serum alkaline phosphatase and bone turnover. Blaxter (12) reported that feeding cows 50 g of iodinated casein daily for 7 weeks did not affect serum calcium, but blood phosphatase activity was increased 20 to 500% above control levels.

Care and associates (30) reported that thyroparathyroidectomy decreased the absorption of calcium from the intestine of sheep. They also found that infusion of tri-iodothyronine did not affect serum calcium. Payne and others (137) found that the defects of calcium metabolism observed after thyroparathyroidectomy in goats were abolished by daily subcutaneous injections of 1 mg thyroxine. Intestinal absorption of calcium was increased to normal levels. Bone accretion rate increased from 3.30 to 8.20 g per day. Controls averaged 5.45 g per day. Exchangeable calcium was increased from 2.9 g to 5.0 g. They reported that a combination of 10 million units vitamin D and

100 mg l-thyroxine intramuscularly for 4 days increased the ability of cows in late pregnancy to counteract hypocalcemia by raising mobilization rate and available reserves to normal levels. Thyroxine therapy (106) eliminated the metastatic calcification observed in some instances after massive vitamin D feeding. This effect was attributed to increased accretion in bone. Todd and associates (169) found that subcutaneous injections of 10 mg thyroxine daily to thyroparathyroidectomized cows maintained milk production at normal levels. Calcium content of milk was not altered. An Arizona report (140) showed that feeding 10 g of iodinated casein to thyroparathyroidectomized cows maintained lactation at levels comparable to controls. There was no difference in milk calcium content.

Role of vitamin D in calcium regulation. Hibbs and coworkers (74) reported that feeding massive doses of 5 to 30 million units of vitamin D during the 5 days prior to parturition significantly reduced the incidence of milk fever. Feeding lower levels for longer periods was not effective (72). Large doses of vitamin D (48) fed to calves for considerable periods caused increased absorption and retention of dietary calcium and eventually death. Conrad and Hansard (34) found that feeding five million units vitamin D for 5 days increased true digestibility of dietary calcium from 47.7% to 69.8% in young growing steers. Endogenous loss dropped from 2.27 to 1.64 g/day. Net retention was increased.

In another report (35) feeding 30 million units of vitamin D for 5 days to dry and lactating cows increased calcium retention in both groups. True digestibility was increased in both groups about 17 percentage units. Vitamin D did not affect milk calcium and phosphorus. Manston (105, 106) found that vitamin D injections of 10 million units

increased absorption and retention of calcium in cattle. Hibbs and Conrad (71) reported that daily feeding of 32,000 units of vitamin D did not increase apparent absorption of calcium from the gut unless phosphorus balance was positive. This was due to unavailability of both calcium and phosphorus in diets causing negative phosphorus balances.

Feeding five million units of vitamin D for 5 days resulted in a four-fold increase in the disappearance rate of intravenous radiocalcium from the blood of growing steers (34). Vitamin D caused increased bone uptake of radiocalcium as well as increased bone calcium mobility. This increase was due to increased absorption as well as direct effects on bone. Manston (105) found that vitamin D increased both bone accretion and resorption but the net effect was to increase bone uptake. Muir and associates (123) studied the effects of feeding small or massive levels of vitamin D on the ability of cows to mobilize body reserves during hypocalcemia. Vitamin D feeding did not significantly alter the size of the mobilizable body reserves. Vitamin D fed cows mobilized reserves at a significantly faster rate than controls. Payne et al. (137) found that massive doses of vitamin D increased the calcium mobilization rate of cows in late pregnancy from 0.50 g per hour to 0.75 g per hour. Available calcium reserves increased to above normal levels. Vitamin D in massive doses depressed parathyroid activity (23) and caused hypertrophy of parafollicular cells (25). Manston (105) and Conrad and Hansard (34) indicated that vitamin D increases bone accretion. It would appear that increased ability to counteract hypocalcemia was a result of both increased absorption and decreased endogenous loss.

Possible role of estrogen in calcium regulation. According to Nurimo (130) estrogen decreased serum calcium and increased calcium absorption in cattle. Payne and others (137) found that estrogen reduced feed intake to about one half original values. Muir and associates (124) concluded that estrogen decreased food intake but had no effect on bone resorption. Oral stilbesterol feeding of lambs resulted in no reduction of feed intake and a significant reduction of endogenous fecal calcium loss (154). Ovariectomy of cattle (138) was followed by a drop of 2 mg/100 ml in serum calcium within 24 hours. The decrease could not be prevented by stilbesterol, progesterone, or testosterone. Fasting normal cows did not produce the same effect.

Payne and associates (137) postulated that high levels of estrogen at parturition accounted for the decreased feed intake reported (119, 120) at that time. This decrease along with bowel stasis (117, 120, 136) accounted for the inability of the parturient cow to regulate serum calcium. Interestingly, hypocalcemia has been produced (118) by injections of oxytocin into estrogen primed sheep. Both hormones are known to be involved in parturition.

Summary. There can be no doubt that the parathyroid and thyroid are directly involved in the regulation of calcium metabolism. Regulation is affected by the interplay of parathormone, calcitonin, and vitamin D. Parathormone promotes mobilization of calcium and calcitonin antagonizes this effect. Vitamin D acts by increasing absorption of calcium. Thyroxine keeps bone cells responsive to actions of other hormones and appeared to have direct effects on bone calcium metabolism. Calcium metabolism in cattle is regulated primarily via the gut and, to

a lesser extent by the skeleton. Regulation is responsive in some way to the needs for calcium, especially for growth and lactation. The kidney rarely functions in an important role in cattle. Although cattle show the characteristic responses to parathormone and calcitonin, hormonal relationships and their importance in the calcium metabolism of cattle are incompletely understood. The roles of thyroxine and calcitonin in calcium metabolism of cattle deserve much further study.

CHAPTER III

EXPERIMENTAL PROCEDURES

Two groups of experiments were conducted to compare various aspects of calcium metabolism in normal and thyroid damaged cattle.

The following procedures were common to all experiments. Specific techniques and alterations have been described under the individual experiments.

Radioiodine thyroid damage in calves was accomplished via single oral doses of 22 to 27 mCi ^{131}I given one to five months prior to experiment. Surgical thyroidectomy was performed approximately three months prior to experiment. No calf subjected to radioiodine damage was considered thyroid-damaged if: its serum protein bound iodine exceeded 3.0 μg per 100 ml (μg/100 ml); its serum thyroxine level exceeded 1.5 μg/100 ml; or the radioiodine uptake by its thyroid, determined at slaughter, exceeded 5.0% of the administered dose. Details of thyroid damage for the adult cattle utilized have been reported (115). Parathormone status was considered normal if serum calcium was in the range 9-12 mg/100 ml.

In all experiments utilizing radioactivity, the calves were confined in metabolism stalls suitably equipped for separate collection of urine and feces. The cows used were kept in dry lot before and after experiments. During experiments they were confined in either stanchions or metabolism stalls.

Both cows and calves had access to medium quality grass-legume hay at all times. Calves received 1 kg of the concentrate mixture described in Table 1 twice daily. Lactating cows received 16% protein dairy pellets,

TABLE 1. Percentage composition of concentrate mixture fed to calves

Ingredient	Percent
Ground yellow corn	74.5
Alfalfa meal (17% DEHY)	5.0
Black strap molasses	5.0
Soybean meal (44%)	14.0
Dicalcium phosphate	1.0
Plain salt	0.5
4400 IU stabilized vitamin A added per kg	

containing non-iodized salt, according to milk production twice daily. Non-lactating cattle received no concentrates. Non-iodized salt and water were available to cows at all times. Animals confined in metabolism stalls were offered water three times daily and were fed twice daily.

The radioactive iodine used in these experiments was carrier free. Radioactive calcium was of high specific activity. Intravenous dosing of both radioactive and non-radioactive material was accomplished via jugular catheterization with polyethylene tubing.[1] Oral doses of radioactivity were administered in gelatin capsules with a balling gun.

Blood samples were collected by jugular puncture and allowed to clot 12 to 24 hours. Serum was separated by centrifugation and stored at 4° C until analyzed. Feces and urine collections were weighed and sampled once daily. To prevent precipitation, urine collections were acidified with 6 N HCl. Feces and urine were stored under refrigeration until analyzed.

Radiochemical analysis of samples for ^{47}Ca and ^{125}I was conducted as follows. One to 3 ml of liquid was pipetted, or 1 to 4 g of solid material was weighed, into counting tubes for radioactivity determinations. Suitable standards prepared from the dosing solutions were counted with the samples to correct for physical decay and to allow expression of results as percentage of the administered dose. The ^{47}Ca and ^{125}I content were determined in a well type scintillation counter.[2] The ^{47}Ca content was determined free of contribution from

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[1]Becton, Dickinson and Company, New York, New York.

[2]Nuclear Instrument and Chemical Corp., Chicago, Illinois.

from its daughter, ^{47}Sc, by counting the portion of the spectrum above 0.69 Mev, the highest energy of ^{47}Sc. The ^{45}Ca of samples was determined from oxalate precipitates by the method of Lyke (104) using an automated beta counting system.[3]

Analyses for calcium and magnesium were conducted on suitable dilutions of ashed samples by atomic absorption spectrophotometry using a Perkin-Elmer 303 atomic absorption spectrophotometer.[4] Phosphorus analysis was by the method of Fiske and Subbarow (55) using either an Evelyn photoelectric colorimeter[5] or a Coleman 44 spectrophotometer. Protein bound iodine was determined by the method of Lennon and Mixner (97). Serum thyroxine levels were assayed by Tetrasorb diagnostic kits.[6] Except for thyroxine levels all analyses were in duplicate.

Appropriate statistical analyses were made according to methods outlined by Steel and Torrie (155). Means are presented with their associated standard errors. Individual data are reported in the appendix tables. Except where otherwise indicated, tests for significance were made at the 0.05 level of probability.

I. ROLE OF THE THYROID IN HYPERCALCEMIA AND AT PARTURITION IN CATTLE

A. Response of Thyroid-damaged and Normal Mature Cattle to Hypercalcemia

Experiment 1. This experiment was conducted to determine if radiation damage of the thyroid gland impaired the ability of cattle to counteract

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[3]Nuclear Instrument and Chemical Corp., Chicago, Illinois.

[4]Perkin-Elmer Corp., Norwalk, Connecticut, manufactured both 303 and Coleman 44 spectrophotometers.

[5]Rubicon Company, Philadelphia, Pennsylvania.

[6]Abbott Laboratories, North Chicago, Illinois.

hypercalcemia. Three mature athyroid cattle averaging 426 ± 58 kg body weight and three normal cattle averaging 421 ± 40 kg received an intravenous infusion of 24 mg calcium per kg body weight as calcium borogluconate solution.[7] Hourly blood samples were taken for 2 hours pre- and 8 hours postinfusion and at 4-hour intervals thereafter up to 24 hours after infusion. Serum calcium and magnesium were determined.

Experiment 2. The purpose of this experiment was to determine the response to hypercalcemia, as in the first experiment, when effects of thyroxine insufficiency were excluded. Five pairs of identical twin cows were used. One member of each pair had radioiodine thyroid damage. To correct for thyroxine insufficiency, four of the thyroid-damaged cows were receiving 8 g per day of commercially prepared iodinated casein[8] which, presumably, contained no calcitonin activity. Since the fifth thyroid-damaged cow showed only slight effects of damage, she did not receive iodinated casein. Average body weights for the control and thyroid-damaged groups were 514 ± 52 and 480 ± 61 kg respectively. Calcium chloride solution (5.5%) was infused into four twin pairs at 11 mg calcium per kg body weight and into the fifth pair at 15 mg per kg. The sampling schedule and procedures were the same as in the Experiment 1. Serum calcium, phosphorus, and magnesium were measured.

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[7]Elanco Products Company, Indianapolis, Indiana. The solution contained: calcium, 13.6 g/l as calcium borogluconate and calcium hypophosphite; phosphorus, 5 g/l as calcium hypophosphite; magnesium, 3 g/l as magnesium chloride; dextrose, 50 g/l.

[8]Protamone, Agri-Tech Chemicals, Kansas City, Missouri.

B. Response of Thyroid-damaged and Normal Calves to Hypercalcemia

The purposes of this experiment were: to determine if replacement therapy would restore to normal the response of thyroid-damaged calves to hypercalcemia; and to compare the response of surgically thyroidectomized and radioiodine thyroid-damaged calves to hypercalcemia when supplemental thyroxine was given. Three normal calves averaging 153 ± 20 kg body weight, three radioiodine thyroid-damaged calves averaging 166 ± 16 kg and three surgically thyroidectomized calves averaging 141 ± 2 kg received 23 mg calcium per kg body weight as 5.5% calcium chloride solution. Radioiodine damage or surgery occurred two to four months prior to test. Beginning 7 days prior to test, thyroid-damaged animals were given 30 mg l-thyroxine on their concentrate feed once daily. Blood samples were taken at 0 and 0.5 hours after infusion, at hourly intervals to 12 hours after infusion, and again at 24 hours. Serum calcium, protein bound iodine and thyroxine levels were determined. Thyroxine was discontinued and 6 weeks later the calves were dosed orally with 25 μCi of ^{125}I and slaughtered 24 hours later. The thyroids were removed, dissected free of fat, digested in concentrated KOH, diluted to a known volume, and ^{125}I content determined. The ^{125}I uptake of the thyroids was used to ascertain the extent of thyroid damage.

C. Effects of Thyroid Damage on Serum Calcium Depression at Parturition

The purpose of this experiment was to investigate the role of the thyroid gland in the changes which occur in serum calcium at parturition. Blood samples were taken from cows one week before expected calving, on the day of calving, and approximately one week after calving. Samples were taken for 12 normal parturitions by four identical twins and their

thyroid-damaged mates and two non-twin pairs of normal and thyroid-damaged cows. Serum calcium was determined using a Unicam S.P. 90 atomic absorption spectrophotometer.[9]

D. Hypocalcemic Activity of Parturient Serum from Normal and Thyroid-damaged Cows

This experiment was an attempt to determine if a calcium lowering principle was circulating in the blood of cows at parturition. One normal and one thyroid-damaged cow were used as donors. One liter of blood was collected from each cow on the day she calved. Blood was immediately refrigerated and allowed to clot. Serum was separated in a refrigerated centrifuge and stored at 4° C until used. Two 12-week-old calves each received intravenous infusions of 250 ml of serum from the normal cow. Blood samples were taken over the subsequent 24 hours and analyzed for calcium content. Since the cows calved one week apart, the same calves received infusions of serum from the thyroid-damaged cow. Dosing procedure was the same. Blood samples were taken at intervals for 24 hours post-infusion and analyzed for calcium.

II. ROLE OF THE THYROID IN NORMAL CALCIUM METABOLISM OF CATTLE

A. Effects of Thyroid Damage on Calcium Metabolism in Growing Calves

Experiment 6. The purpose of this experiment was to determine the effects thyroid damage would have on the calcium metabolism of growing calves. Three radioiodine thyroid-damaged calves averaging 138 ± 3 kg body weight and three considerably younger normal calves averaging

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[9]Pye-Unicam Ltd., New Orleans, Louisiana.

94 ± 3 kg were placed in metabolism stalls. Radioiodine administration occurred five weeks prior to test. Daily intake of hay and concentrates was recorded for 5 days. Then all calves were dosed simultaneously with approximately 100 μCi ^{47}Ca intravenously and approximately 500 μCi of ^{45}Ca and 200 μCi ^{125}I orally. Concurrent 5-day chemical and radiochemical balance studies were conducted. Blood samples were taken at 0, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours after dosing and at 24-hour intervals to 120 hours after dosing. Serum calcium, phosphorus, magnesium, and radionuclide content were determined. Calves were offered 2000 g of mixed grass-legume hay and 2000 g of concentrate daily in equal feedings at 8:00 a.m. and 4:00 p.m. Weigh backs of hay and grain were taken twice daily, before feeding. Daily hay and grain samples were composited for analysis.

The calves were slaughtered at 120 hours after dosing, the digestive tracts were removed, the eighth rib and femur were taken from the left sides, and the thyroids were recovered. Thyroids were treated as in IB. Each gastrointestinal tract was divided into rumen-reticulum, omasum, abomasum, three small intestine sections of equal length, cecum, and two sections of large intestine of equal length. Contents of each section were recovered, weighed, and sampled. Bones were ashed for 24 hours at 600° C, and the ash dissolved in 6 N HCl. Radiochemical content was determined by counting known amounts of samples or known dilutions of ashed samples. Stable minerals in feed, feces, and ingesta were determined on suitable dilutions of ashed samples. Serum protein bound iodine and thyroxine were determined. Daily calcium, phosphorus, and magnesium balances were calculated.

Calcium specific activity was determined by dividing the percentage of the dose in the sample by the calcium content expressed as grams. The "available calcium" pool of the body was obtained by modifying the method of Luick and associates (102). Briefly, a semilogarithmic plot of serum ^{47}Ca specific activity on time was made. Utilizing the data from the linear portion (12 to 48 hours) of this curve, linear regression analysis of log of serum calcium on time was used to predict the value of blood ^{47}Ca specific activity at time zero, which value would have been obtained had the injected radiocalcium equilibrated instantaneously within all body pools. Dividing the zero time specific activity into 100% of the radiocalcium dose gave the grams of calcium in the equilibrating "available calcium" body pool. The "available calcium" pool half-time was calculated from the regression equations by setting the value of serum specific activity equal to one half the zero time value and solving for time. It is a measure of the rate at which the "available calcium" pool is turning over.

Estimation of endogenous fecal calcium (E) in grams, that portion of fecal calcium of body rather than dietary origin, was made by the method of Manston (105) as in equation 1 for the last 2 days of the balance period.

$$[1] \quad E = \frac{\%\ ^{47}Ca \text{ dose in feces daily}}{^{47}Ca \text{ specific activity of serum}}$$

E was then used to calculate the true digestibility (TD) of calcium according to Hansard, Crowder, and Lyke (68) as in equation 2.

$$[2] \quad TD = 100 - \frac{\text{Fecal calcium (g) - E (g)}}{\text{Calcium intake (g)}} \times 100$$

True absorption (A) of orally administered radiocalcium was calculated as in equation 3, where CF is the cumulative percentage of the oral dose recovered in the feces and B is the total fraction of intravenous

radiocalcium recovered in the feces.

$$[3] \quad A = \frac{100 - CF}{1 - B}$$

The percentage of the oral dose retained was calculated by subtracting the total percentage of the oral radiocalcium dose excreted in the urine from that absorbed. The percentage of the absorbed dose retained (R) was calculated as in equation 4, where A is true absorption from equation 3 and U is the urinary excretion of oral radiocalcium.

$$[4] \quad R = \frac{A - U}{A} \times 100$$

Experiment 7. The purpose of this experiment was to repeat the design of Experiment 6 using calves with thyroid damage of longer duration. Two radioiodine thyroid-damaged calves, which were treated four months prior to test, averaging 162 ± 16 kg body weight and two normal calves averaging 142 ± 10 kg were used. In addition to intravenous ^{47}Ca, the calves were subjected to transient hypercalcemia induced by administering 15 mg calcium per kg body weight as 5.5% calcium chloride solution. Oral ^{45}Ca and ^{125}I were also administered. Concurrent stable and radiochemical balances were conducted as in Experiment 6. Blood samples were taken at 0, 0.5, 1, 2, 3, 4, 5, 6, 8, 10, and 24 hours and at 24-hour intervals to 120 hours after dosing. Samples were handled as described in Experiment 6. The calves were sacrificed 144 hours after dosing and processed as in Experiment 6. Due to erratic feed intake fluctuations, the daily offering of concentrate and hay varied. Feeding, weigh back, and sampling regimens were the same as in Experiment 6. Balance results and other estimates were calculated as discussed in Experiment 6.

Experiment 8. The purpose of this experiment was to determine the effects of thyroxine therapy on the metabolism of calcium by thyroid-damaged calves and their response to hypercalcemia. Three radioiodine thyroid-damaged calves (treated four months prior to test) averaging 154 ± 3 kg body weight and three control calves averaging 139 ± 5 kg were used in a three part experiment. In Part 1, hypercalcemia was induced by infusion of 15 mg calcium per kg body weight as 5.5% calcium chloride solution. Blood samples were taken at 0, 0.5, 1, 2, 3, 4, 5, 6, 8, 10, and 24 hours postinfusion. Serum calcium, phosphorus, and magnesium were measured. In Part 2, the thyroid-damaged calves were given daily subcutaneous injections of 3 mg l-thyroxine for 5 days prior to and throughout the balance period. The diet, feeding, weigh back, and sampling procedures were the same as in Experiment 6 except that the daily offering of hay was 2400 g. The calves received an intravenous infusion of 5.5% calcium chloride as in Part 1, 100 μCi ^{47}Ca; and concurrent 5-day stable and radiochemical balances were conducted. Blood samples were taken at 0, 0.5, 1, 2, 3, 4, 5, 6, 8, 10, 12, and 24 hours after dosing and at 24-hour intervals to 120 hours. Calcium, phosphorus, magnesium, and ^{47}Ca content of serum, urine, and feces were measured. Balance data were calculated as in Experiment 6.

The calves were maintained on thyroxine and stable feed intake for 12 days after the completion of Part 2. In Part 3 they received an oral dose of approximately 500 μCi ^{45}Ca and 150 μCi of ^{125}I. A second 5-day balance period was conducted. Blood samples were taken at 0, 4, 10.5, and 24 hours after dosing and at 24-hour intervals to 120 hours. The calves were slaughtered 120 hours after dosing and samples taken and analyzed as in Experiment 6. Balance results were calculated as in

Experiment 6. In calculating true digestibility, the daily calcium intake and excretion values used were the average of those obtained in the two balance period.

B. Effects of Thyroid Status and Thyroxine Therapy on Calcium Metabolism in Lactating Cows

Experiment 9. The purpose of this experiment was to determine the effect of accelerated thyroid activity on the utilization of calcium in milk secretion. One athyroid and one normal cow producing approximately 6 and 10 kg milk daily were used in two trials. In the first trial, the cows received approximately 190 μCi of ^{47}Ca as a single intravenous dose immediately after milking. Samples were taken over the subsequent 5 days. Feces and urine were handled as discussed previously. Blood samples were taken just after milking at 8:00 a.m. and 4:00 p.m. Milk was weighed and sampled at each milking and stored under refrigeration until analyzed. The ratio percent dose per ml of milk : percent dose per ml of serum was calculated and used as an estimate of transfer of blood calcium to milk. In the second trial, the cows received a single intravenous dose of approximately 250 μCi of ^{47}Ca and samples were taken as in the first trial. Immediately before dosing and at the subsequent four milkings the cows received 1 mg of partially purified thyroid stimulating hormone[10] intravenously. Results were calculated as in the first trial.

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[10]Supplied by the Pituitary Hormone Distribution Program, Endocrinology Study Section, National Institute of Arthritis and Metabolic Diseases, Washington, D. C.

Experiment 10. The purpose of this experiment was to determine the effects of thyroid damage and thyroxine therapy on the utilization of calcium in milk secretion. One athyroid and two normal cows were used in two trials. In the first trial, the athyroid cow received 5 mg l-thyroxine subcutaneously daily for 15 days prior to and throughout the trial. In the second trial no thyroxine therapy was given. After an adjustment period, the cows were dosed immediately after a morning milking with approximately 1 mCi of ^{45}Ca intravenously. Samples were taken as in Experiment 9 over the next 7 days in Trial 1 and for 5 days in Trial 2. Stable and radiocalcium content of feces and milk were determined on suitable dilutions of ashed samples. Serum and urine calcium were measured. Radioactivity of serum and urine was determined by drying a measured amount of sample in planchets and counting with suitable standards mixed with unlabeled serum or urine and dried. Results expressed as milk to serum ratio of radioactivity and as specific activity of serum and milk were analyzed. Endogenous fecal calcium was determined as in Experiment 6.

C. Placental Transfer of Calcium in Thyroid-damaged and Normal Cattle

The objective of this experiment was to determine whether lack of the thyroid affected the placental transfer of calcium during the last 20 days of gestation. Three athyroid and three normal cows were dosed intravenously with ^{45}Ca from 7 to 20 days before calving. Calves were sacrificed at birth and dissected for analysis. Bones were ashed, dissolved in 6 N HCl, and activity was determined in known dilutions of ash. The skin and the gut and internal organs were macerated in nitric acid. This mixture was weighed, samples taken and ashed, and radioactivity

was determined as with bones. Meat was separated from the bones, ground, weighed, and representative samples ashed for analysis. Total percentage of the dam's dose in the fetus was calculated.

CHAPTER IV

RESULTS AND DISCUSSION

I. ROLE OF THE THYROID IN HYPERCALCEMIA AND AT PARTURITION IN CATTLE

A. Response of Thyroid-damaged and Normal Mature Cattle to Hypercalcemia

Experiment 1. The assumption in this experiment was that the thyroid-damaged cattle would be deficient in calcitonin. Results of this experiment are shown in Figure 1. The overall standard error in this and other experiments was calculated from the residual variation after hour effects had been removed.

The magnesium infusion was 5 mg per kg body weight. Serum magnesium levels of thyroid-damaged cattle were consistently higher before infusion, increased to higher levels after infusion, and declined at a slightly slower rate than controls. These differences are not considered biologically significant.

There was no significant difference in preinfusion serum calcium levels between groups. Thyroid-damaged cattle had slightly higher serum calcium 1 hour after intravenous calcium infusion than controls, 16.9 vs 16.4 mg/100 ml. Expressed as a percentage of initial values, the thyroid-damaged and control values 1 hour after infusion were 172 and 161. From 2 to 8 hours after infusion, serum calcium of controls was lower than that of thyroid-damaged cattle, which finding indicated that the response to hypercalcemia was impaired by lack of a functional thyroid. However, these differences were not statistically significant at the .05 level of probability. The consistent differences in treatment means could

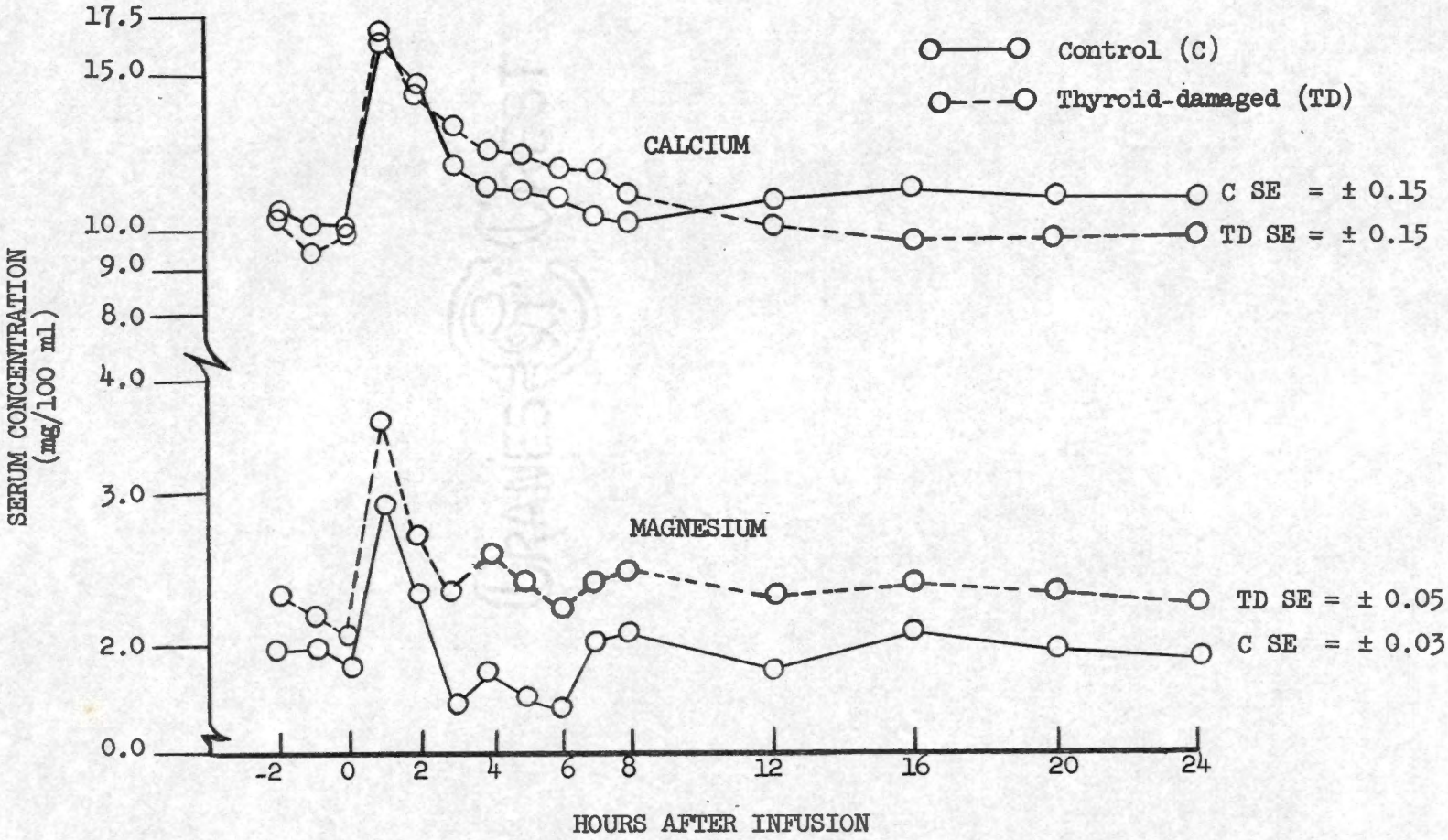

Figure 1. Average serum calcium and magnesium responses of three thyroid-damaged and three control cattle used in Experiment 1 to intravenous infusion of 24 mg calcium/kg body weight as calcium borogluconate solution.

indicate that the failure to demonstrate significant differences was due to small numbers rather than lack of treatment effects. After eight hours serum calcium of controls was consistently higher than that of thyroid-damaged cattle but the difference was not significant. Serum calcium of both groups was within the normal range 7 hours after infusion. From 1 to 2 hours after dosing no defect was apparent.

Linear regression analysis of log serum calcium on time after dosing over the first four hourly samples accounted for 93 and 99% of the variation in the serum calcium levels of thyroid-damaged and control groups respectively. Log serum calcium was a simple linear function of time. Therefore, serum calcium declined as a single exponential function of time. The equation has the form $Y = AB^X$, where Y is the serum calcium in mg/100 ml, A is zero time value, X is time after dosing in hours, and B, a form of the constant e^b, has the units $hours^{-1}$ and is the result of the interaction of all factors which lower serum calcium and factors which raise it. Theoretically, normal cows have the optimal clearance rate, B value. Deviations from such values represent changes in the balance of the opposing groups of factors. Regression coefficients for the thyroid-damaged and control groups were -0.045 and -0.059. These coefficients were significantly different ($P < .01$). The constants were 0.90 and 0.87 respectively. Loss of the thyroid resulted in a significantly slower removal of calcium from the blood over the first 4 hours. This finding and the consistently higher serum calcium levels in athyroid cattle as compared to controls indicate a defect in calcium clearance was present. No measure of thyroid status was made in this trial. However, previous tests had shown that the three thyroid-damaged cattle were athyroid.

Experiment 2. The results of this experiment are shown in Figure 2. Since both infusion solution and the amount of calcium infused per kg of body weight differed between the experiments, Experiments 1 and 2 are not directly comparable. In Experiment 2, four of the five thyroid-damaged cows received 8 g of iodinated casein once daily. Since neither member of the fifth pair differed from the other members of her group, they were averaged with the other members of their respective groups. The iodinated casein was adequate but not excessive as judged by heart rates and milk production. It was expected that defects in response to hypercalcemia would have been due solely to calcitonin deficiency.

Average serum magnesium levels were not different between groups, were consistently higher than in Experiment 1, were barely within normal range, and rose in later hours to above normal levels. Phosphorus levels began to decline 1 hour after infusion and had stabilized at lower levels 5 hours after infusion. No effects of thyroid damage on magnesium or phosphorus were evident.

The serum calcium response of the groups showed no consistent difference due to thyroid status. There was no significant difference in preinfusion serum calcium of the thyroid-damaged and control groups. There was no difference between groups in serum calcium 1 hour after infusion. Serum calcium of thyroid-damaged cows averaged lower 2, 3, and 4 hours after infusion than controls, but 6, 7, and 8 hours after infusion the reverse was true. These differences were not significant ($P > .05$). Serum calcium had returned to preinfusion levels 7 hours after infusion. Linear regression analysis of the data, as in Experiment 1, accounted for 94 and 96% of all variation in serum calcium in the thyroid-damaged and control groups respectively. The regression

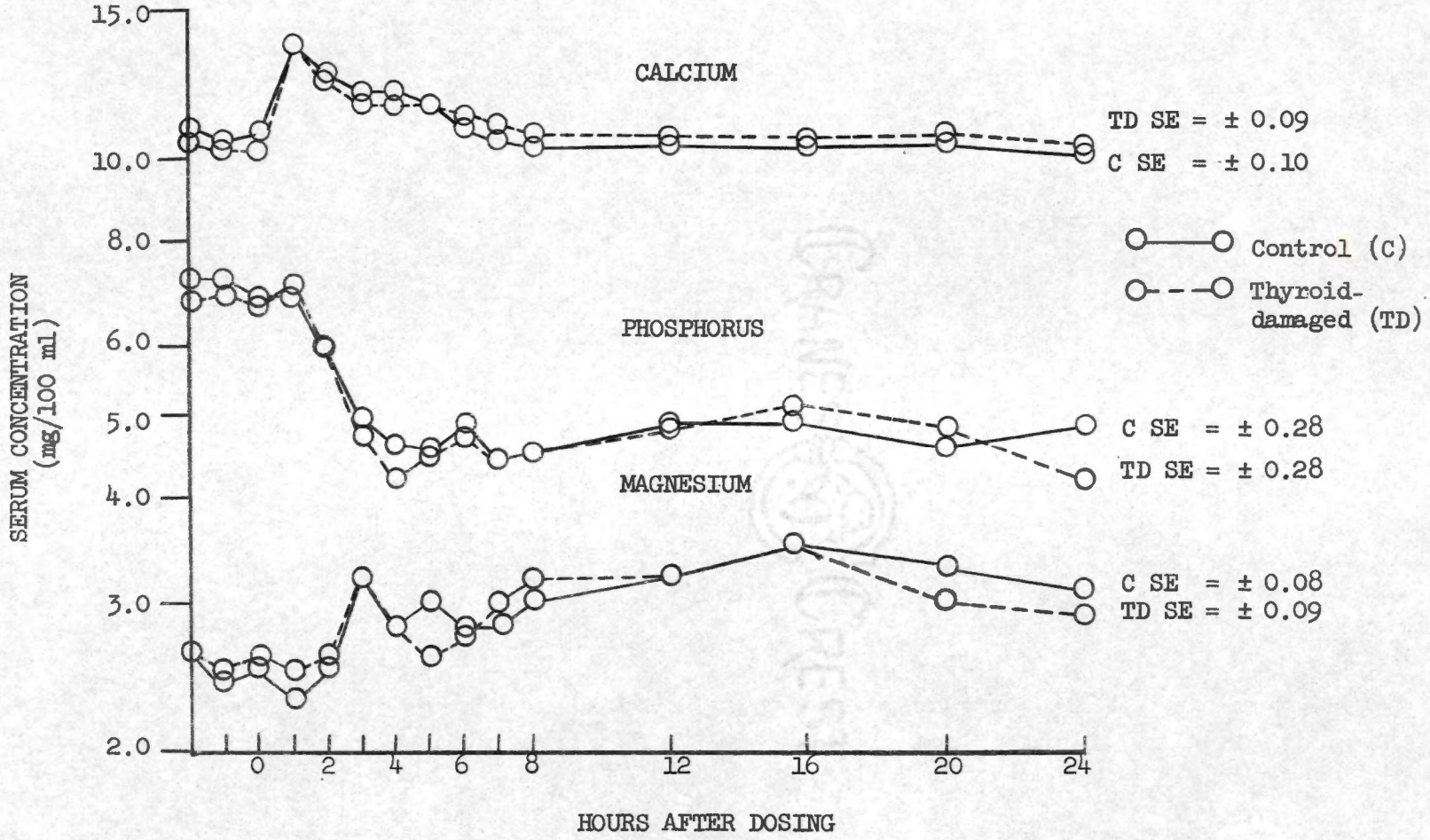

Figure 2. Average serum calcium, phosphorus, and magnesium responses of five iodinated casein supplemented thyroid-damaged, and five control cows used in Experiment 2 to intravenous infusion of 11 mg calcium/kg body weight as 5.5% calcium chloride solution.

coefficient for the thyroid-damaged group, -0.030, was significantly ($P < .01$) larger than that for the controls, -0.018. Constants were 0.93 and 0.96. Thyroid-damaged cows given iodinated casein had normal or above normal ability to respond to hypercalcemia. No defect related to calcitonin was evident.

In the control group, two cows in late lactation produced an average of 1.8 kg of milk for the 8 hours after infusion. Two other cows in mid-lactation produced an average of 3.7 kg for the same period. Serum calcium values 2, 4, and 6 hours after infusion, expressed as a percentage of the preinfusion level, averaged 117, 115, and 103 for the lower producers and 110, 109, and 98 for the higher producers. A 106% increase in milk production was associated with an average 6% decrease in the level of serum calcium. Similar calculations on the two lactating cows in the thyroid-damaged group showed that serum calcium of a cow which produced 3.4 kg of milk over the 8 hours after infusion averaged only 2% greater for the three hourly comparisons than that of a cow which produced 9.6 kg of milk in the same period, a 180% increase. These results indicate that level of milk production was not a major factor controlling the clearance of calcium from blood.

B. Response of Thyroid-damaged and Normal Calves to Hypercalcemia

The results of this experiment are shown in Figure 3. Serum calcium was determined on samples pooled by treatment groups of three calves each. Complete removal of the thyroid was accomplished by surgery. This was verified at slaughter. The extent of radioiodine thyroid damage was determined by 24-hour ^{125}I uptake at slaughter which averaged 17.70 ± 5.34% of the dose in controls but only 0.14 ± 0.01% of the dose in radioiodine thyroid-damaged calves.

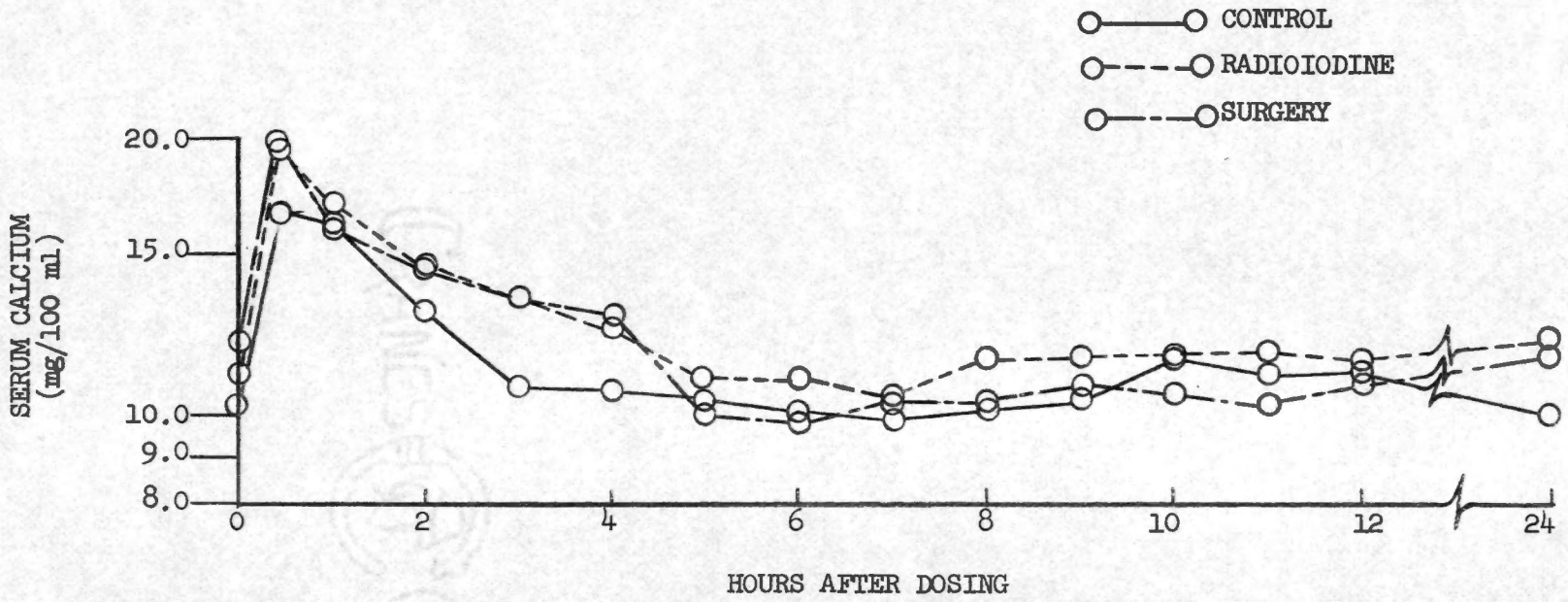

Figure 3. Serum calcium response of three thyroxine supplemented radioiodine thyroid-damaged, three surgically thyroidectomized, and three unsupplemented control calves to intravenous infusion of 23 mg calcium/kg body weight as 5.5% calcium chloride solution.

Thyroid-damaged calves received oral thyroxine daily; so differences in response would, theoretically, have been due to calcitonin deficiency. The protein bound iodine and circulating thyroxine levels, expressed as μg/100 ml, averaged 5.57 ± 2.19 and 5.77 ± 0.89; 24.93 ± 5.34 and 10.33 ± 0.94, and 24.03 ± 3.77 and 9.17 ± 1.57 for the control, radioiodine thyroid-damaged, and surgically thyroidectomized groups respectively. In giving thyroxine therapy an attempt was made to supply as much absorbed thyroxine activity daily as was reported to be liberated from the thyroid daily (100, 142). Thyroxine therapy was actually excessive.

Radioiodine and surgery groups had higher preinfusion serum calcium levels than controls, and both groups had higher serum calcium levels 0.5 hour after infusion than controls, 19.30 and 19.74 vs 16.65 mg/100 ml. Serum calcium levels were within the normal range 5 hours after dosing. Thereafter there was little change and no apparent treatment differences. Serum calcium was slightly below original levels for the rest of the trial. The higher serum calcium levels 0.5 hour postinfusion in the damaged groups were due primarily to differences in initial serum calcium. Expressed as percentages of the respective preinfusion calcium levels, the values for control, radioiodine, and surgery groups were 163, 177, and 163. Linear regression as described above accounted for 97, 96, and 93% of all variation in the serum calcium levels of control, radioiodine, and surgery groups respectively. Regression coefficients were -0.063, -0.050, and -0.051 for the groups and were not significantly different. Expressing the decline in serum calcium over the first 5 hours as a percentage of the 0.5 hour value revealed no consistent treatment differences. No calcitonin defect was apparent.

The hyperthyroid state of the supplemented animals could have masked such a defect. However, two other possibilities must be considered. The first is that thyroxine therapy completely remedied the defect, but hyperthyroidism did not enhance the ability of calves to counteract hypercalcemia. The second is that no defect was present in the damaged animals. Further study of the problem was undertaken by examining responses to hypercalcemia in calves in other experiments. Figures 4, 5, and 6 show the results of calcium infusion studies made during three other experiments.

The data in Figure 4 were collected in the Part 1 of Experiment 8. Serum protein bound iodine and circulating thyroxine levels, in μg/100 ml, averaged 1.37 ± 0.20 and 0.43 ± 0.04, and 5.53 ± 1.16 and 5.78 ± 0.25 for the thyroid damaged and control calves respectively. There was no significant difference in serum inorganic phosphorus between groups. In the first 5 hours phosphorus levels averaged higher for thyroid-damaged than for control calves. After that, phosphorus levels of controls were higher than those of thyroid-damaged calves. Magnesium levels were at the upper limit of the normal range. There was a trend for serum magnesium to be higher in thyroid-damaged calves than in controls.

Thyroid-damaged calves had higher serum calcium levels, 10.00 mg/100 ml, than controls, 9.28 mg/100 ml, before infusion and higher 0.5 hour values than controls 12.07 vs 11.40 mg/100 ml. Differences in initial serum calcium levels were primarily responsible for the significantly ($P < .05$) lower serum calcium of controls as compared to thyroid-damaged calves for the 4 hours after dosing. Expressed as a percentage of the initial level the 0.5 hour values were 121 and 123 for the thyroid-damaged and control groups respectively. Serum calcium was within the

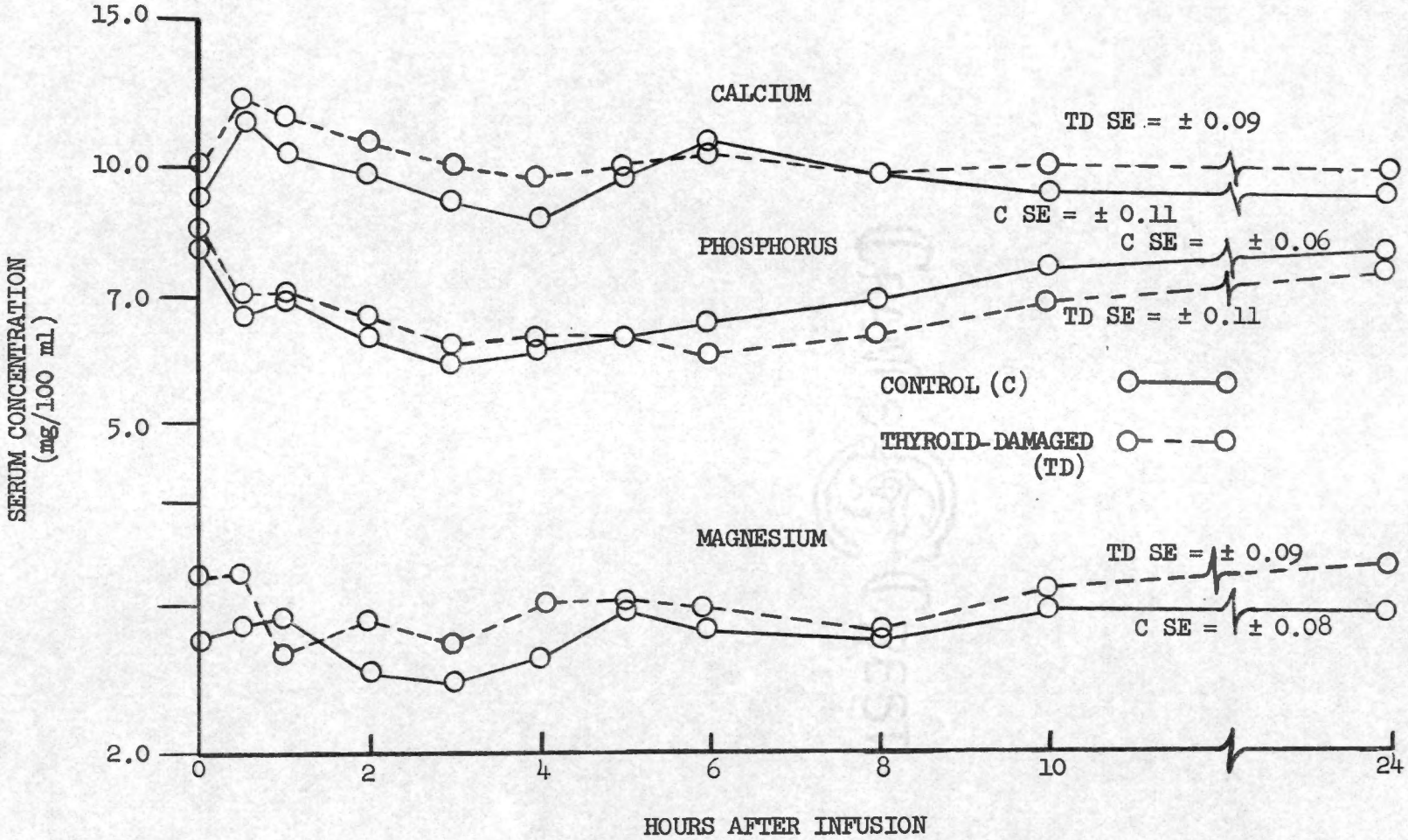

Figure 4. Average serum calcium, phosphorus, and magnesium responses of three thyroid-damaged and three control calves used in Part 1 of Experiment 8 to intravenous infusion of 15 mg calcium/kg body weight as 5.5% calcium chloride solution.

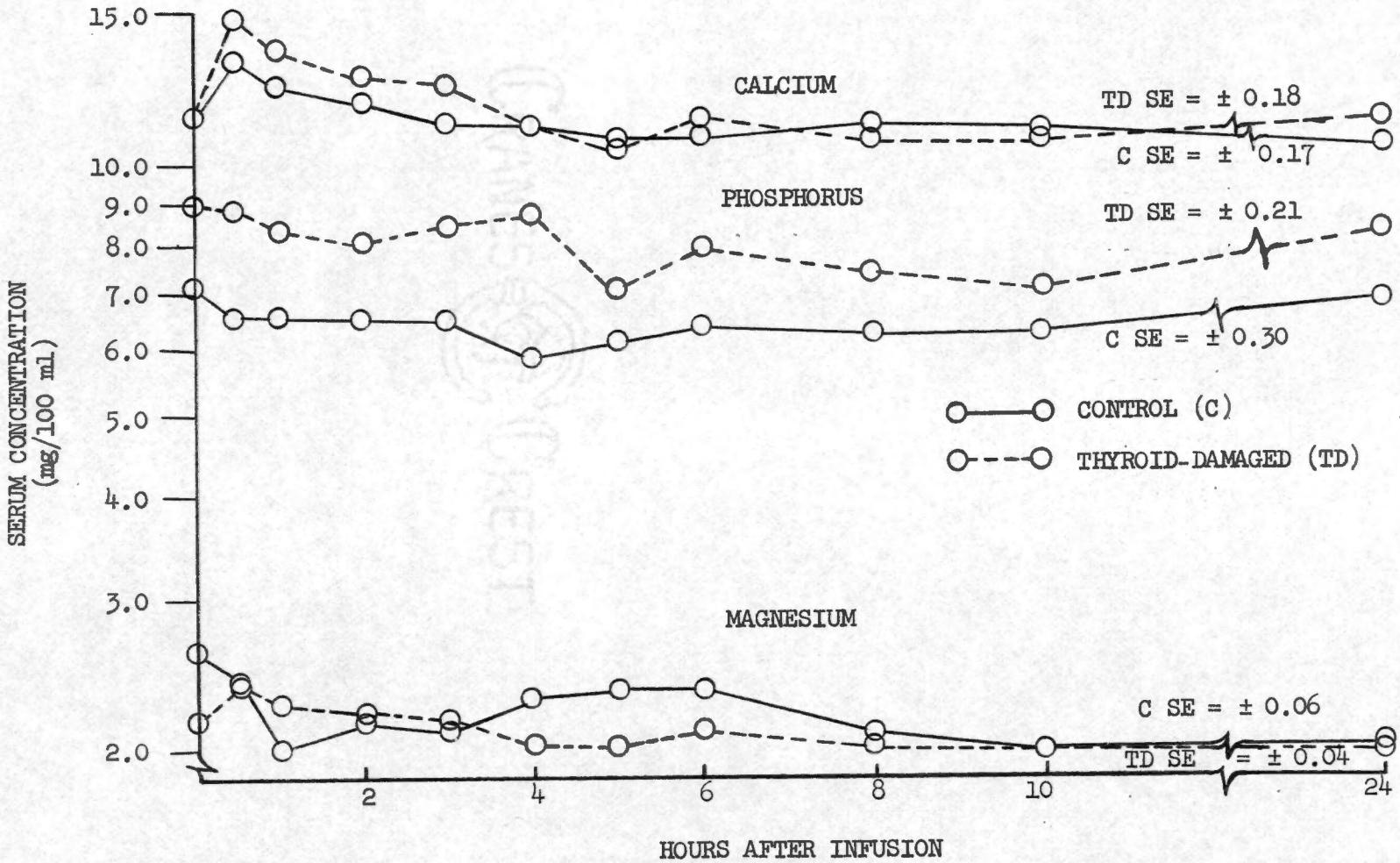

Figure 5. Average serum calcium, phosphorus, and magnesium responses of two thyroid-damaged and two control calves used in Experiment 7 to intravenous infusion of 15 mg calcium/kg body weight as 5.5% calcium chloride solution.

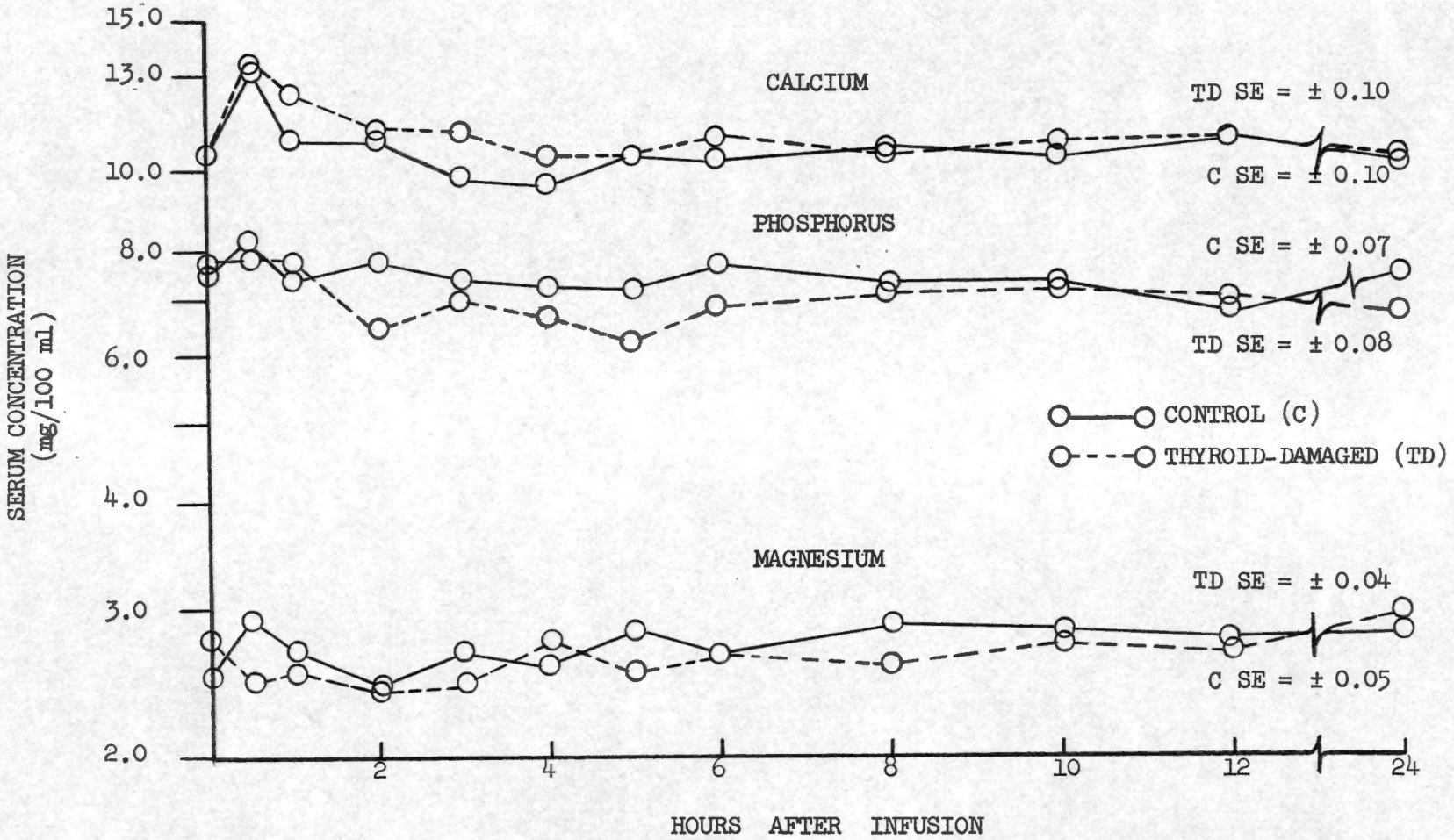

Figure 6. Average serum calcium, phosphorus, and magnesium responses of three thyroxine supplemented thyroid-damaged and three unsupplemented control calves used in Part 2 of Experiment 8 to intravenous infusion of 15 mg calcium/kg body weight as 5.5% calcium chloride solution.

normal range 2 hours after dosing. Linear regression as above accounted for more than 99% of the variation in serum calcium of both groups. The regression coefficients for the thyroid-damaged group, -0.027, and the control group, -0.032, were significantly different ($P < .01$).

Some data collected during Experiment 7 are presented in Figure 5. Serum protein bound iodine of thyroid-damaged calves averaged 1.75 ± 1.15 μg/100 ml, but protein bound iodine and circulating thyroxine levels of controls averaged 7.10 ± 0.10 and 10.31 ± 0.29 μg/100 ml. The control calves were actually hyperthyroid. No consistent treatment effects on magnesium were evident. Serum phosphorus levels of controls were consistently lower than those of thyroid-damaged calves during the trial. These differences were not statistically significant ($P > .05$). No effects of intravenous calcium infusion on serum phosphorus or magnesium were noted. Preinfusion serum calcium of the groups was not different. Serum calcium levels 0.5 hour after infusion averaged higher for the thyroid-damaged calves than for controls, 14.77 vs 12.58 mg/100 ml. Expressed as percentage of the preinfusion serum calcium, the values were 133 and 113. Serum calcium values remained higher in the thyroid-damaged calves for the first 3 hours, but the differences were not statistically significant. Thereafter calcium levels were not consistently different and were within the normal range.

Linear regression analysis as above showed that more than 99% of the within group variation in serum calcium was due to time. The regression coefficients for thyroid-damaged and control calves were -0.032, and -0.019. These coefficients were significantly different ($P < .01$).

The data in Figure 6 were taken in Part 2 of Experiment 8. The subcutaneous daily thyroxine injections resulted in serum protein bound

iodine and thyroxine levels averaging 16.37 ± 0.64 and 20.79 ± 1.95 μg/100 ml in thyroid-damaged calves. Corresponding values for controls were 5.53 ± 1.16 and 5.78 ± 0.25 μg/100 ml. The thyroid-damaged calves were hyperthyroid.

There were no apparent treatment effects on serum magnesium, and no effects of intravenous calcium infusion on magnesium were noted. Serum phosphorus of thyroid-damaged calves averaged lower than controls 2 to 10 hours after infusion. These differences were not consistently significant ($P > .05$). Preinfusion serum calcium levels were not significantly different. Serum calcium levels of thyroid-damaged calves were not significantly higher than controls 0.5 hour after injection, 13.53 vs 13.18 mg/100 ml. Serum calcium was within the normal range 2 hours after infusion. Expressed as a percentage of the initial serum calcium levels the values were 131 and 128 for the thyroid-damaged and control groups. Linear regression of serum calcium levels on time accounted for 96% of the variation in the thyroid-damaged group but only 89% in the controls. The regression coefficients for the thyroid-damaged calves, -0.030, and the controls, -0.034, did not differ significantly. Serum calcium levels of the thyroid-damaged groups were higher than controls for the first 5 hours, but the differences were not statistically significant. Thereafter there were no consistent differences.

Conclusions on the basis of regression analyses must be qualified. The high efficiency of regression in removing variation, as indicated by the large R^2 values, has the effect of making small, biologically unimportant, differences between treatments statistically significant. This may well be the case in data shown in Figure 4, page 54. Removing the

differences in initial serum calcium levels by expressing the data as a percentage of that value, abolished the apparent difference between groups. Such values for the first 4 hours were 121, 116, 107, 101, and 98 for the thyroid-damaged calves and 123, 112, 106, 99, and 95 for controls. In this case the significant difference in disappearance rates is of little physiological significance. No effect attributable to calcitonin was evident. Much the same situation may exist in the data shown in Figure 3, page 51.

In Experiment 1 the difference seen 2 to 8 hours after infusion was not evident in the first two hourly samples. Theoretically the high calcium levels shortly after infusion would stimulate secretion of calcitonin in controls with resultant lower calcium levels. Since no difference between groups existed, factors other than calcitonin may have been controlling the exit of calcium from the blood. Equilibration with extracellular and soft tissue calcium pools, as suggested by others (65) could be occurring. However, calves infused with calcium, Figure 3, did not show the same response as cows even though serum calcium levels were higher than in Experiment 1.

In Experiment 2 the animals were not in a hyperthyroid state. The faster clearance of blood calcium in thyroid-damaged cows than in controls, as indicated by regression analysis and lower average serum calcium values, during the first 4 hours after infusion was offset in the subsequent 4 hours by faster disappearance of calcium from the blood of controls than from blood of thyroid-damaged cattle, as indicated by lower average serum calcium in the former group. As a result no difference due to treatments was noted. Therefore, regression coefficients reported do not represent the total response. Nevertheless, they indicated that

during the period when highest calcitonin stimulation would be expected the cattle with adequate thyroxine but, presumably, no calcitonin removed excess calcium faster than cattle with a source of both hormones.

The data in Figure 5, page 55, present an unusual situation. Although serum calcium levels were higher in thyroid-damaged calves after infusion, the rate of clearance of injected calcium was faster in this group than in controls. Control calves in this experiment cleared calcium at a slower rate than in other trials. Since controls in other experiments, Figure 4, page 54, cleared calcium more rapidly at lower serum calcium levels, an effect of serum calcium level on disappearance rate in this experiment was unlikely. Hyperthyroidism is known to stimulate the turnover of bone calcium (3, 13, 59, 83, 91, 106). Overall increased bone sensitivity to calcitonin due to increased resorption stimulated by thyroxine, as reported by others (176), could account for the lower 0.5 hour levels in control than in thyroid-damaged calves. The slower clearance rate of controls as compared to thyroid-damaged calves could be due to effects of thyroxine on net bone calcium turnover as reported by Burkhart and Jowsey (21).

The differences in Figure 4 and Figure 6, page 56, indicated that thyroxine therapy changed the response to hypercalcemia. In Figure 6 the control preinfusion serum calcium values were as high as those of the thyroid-damaged calves. The failure to show significant differences in regression coefficients could have been due to either a real lack of difference or, more likely, to larger residual variation after regression in controls. These hyperthyroxine thyroid-damaged calves could not counteract hypercalcemia as well as they had before therapy. Excess thyroxine acting on the large areas of active mineralization could stimulate

large increases in bone resorption and formation. Thyroxine was reported to affect such changes in mature dogs (3), cattle (12), and in hypothyroid humans (2, 81). In the normal situation blood calcium is not altered because accretion and, to some extent, excretion counterbalance resorption. Prolonged severe hyperthyroidism in sheep did not alter serum calcium (13). The same was true of cattle (12). In thyroid-damaged calves calcitonin was not available to inhibit the resorption of bone. When more calcium was added by infusion, removal from the blood was dependent on the uptake by bone and the rate of excretion from the body. The same type of mechanism, although less severe, may have been operating in the experiment shown in Figure 3, page 51. Mild hyperthyroidism could have stimulated net bone formation of sufficient quantity to remove the injected calcium. In this case calcitonin would not have been required for hypocalcemic activity. Thyroidectomized goats given 1 mg of thyroxine subcutaneously daily stored more calcium in bones than controls (137). Injections of 2 mg per day increased storage to almost two times control values.

In all of the tests serum calcium levels dropped below preinfusion values and subsequently rose to normal or near normal levels within 24 hours. This secondary rise may have been due to parathormone secretion stimulated by falling serum calcium levels. The large fall in serum phosphorus levels in Experiment 2 could be interpreted as support for this theory. However, the variation in serum phosphorus levels in other experiments and the lack of a definite hypophosphatemia following calcium infusion argue against increased parathormone secretion alone as the cause. Age differences in the animals in Experiments 1 and 2 and those in the other experiments are partially responsible for the differences seen.

Neither thyroid damage nor calcium infusion affected serum phosphorus or magnesium consistently.

These experiments have shown that the role, if any, of calcitonin in the response of cattle to hypercalcemia is not a critical one. The apparent defect in Experiment 1 was not repeated in Experiment 2 where thyroxine therapy was adequate. Hyperthyroidism in athyroid calves restored the response to hypercalcemia to normal. A reasonable explanation for this finding does not require calcitonin. Alternatively, an extrathyroidal source of calcitonin, such as postulated for man (63), and a need for thyroxine induced bone responsiveness as a prerequisite for calcitonin action (83, 114) could cause the results observed in Experiments 2 and 3. A defect in the hypercalcemic response of thyroid-damaged calves could not be conclusively demonstrated. Interactions of thyroxine and calcitonin could be responsible for the varied results. Lavror and Barlet (93) reported that calves were not as responsive to calcitonin as older cows. However, their report is at variance with the work of Care and Duncan (28) who found young lambs more responsive to calcitonin than older sheep.

C. Effects of Thyroid Damage on Serum Calcium Depression at Parturition

The results of this study are presented in Table 2. The serum calcium of controls was significantly less ($P < .01$) than that of the thyroid-damaged cows one week precalving, on the day of calving, and one week postcalving. Within the control group, serum calcium on the day of calving was significantly less ($P < .01$) than precalving values. No significant differences in the postcalving and calving samples were noted. Although serum calcium had not returned to precalving levels a week postcalving,

TABLE 2. Serum calcium, phosphorus, and magnesium changes in thyroid-damaged and control cattle at parturition[1]

Identity	Control	Thyroid-damaged
Serum calcium (mg/100 ml)		
Precalving	9.46 ± 0.13	10.38 ± 0.19
Calving	7.97 ± 0.24	9.48 ± 0.43
Postcalving	8.57 ± 0.77	9.91 ± 0.36
Serum phosphorus (mg/100 ml)		
Precalving	6.24 ± 1.00	6.52 ± 0.82
Calving	5.80 ± 0.82	5.17 ± 0.65
Postcalving	5.42 ± 0.88	6.30 ± 0.89
Serum magnesium (mg/100 ml)		
Precalving	2.43 ± 0.14	2.36 ± 0.14
Calving	2.75 ± 0.14	3.08 ± 0.29
Postcalving	2.42 ± 0.15	2.54 ± 0.05

[1]Each value is the mean of six cows per treatment ± SE.

there was no significant difference between times. Within the thyroid-damaged group, there were no significant differences in any of the serum calcium comparisons. There were no effects of thyroid status or sample time on serum phosphorus. Serum magnesium levels were significantly higher ($P < .05$) on the day of calving than before and after calving. This effect was independent of thyroid status. There were no treatment effects on serum magnesium.

The thyroid was necessary for the drop in serum calcium at parturition seen here. Others have reported such decreases (16, 17, 110, 137). The release of calcitonin in large quantities at parturition proposed by Capen and Young (24) could have been the reason for the drop. Miller and associates (116) reported protein bound iodine levels were normal at parturition in cattle, which finding tends to rule out thyroxine as the cause.

D. Hypocalcemic Activity of Parturient Serum from Normal and Thyroid-damaged Cows

Results of this study are shown in Figure 7. Serum calcium of the normal donor cow at parturition was 8.00 mg/100 ml. Blood samples were taken from the calves immediately before and after infusion. Average serum calcium level of the calves before infusion was 10.03 mg/100 ml. After infusion the value had dropped to 9.26 mg/100 ml. At 2 hours after infusion the value had dropped to 8.06 mg/100 ml. Calcium levels had not returned to normal 24 hours after dosing. The second donor cow was thyroid-damaged and had a serum calcium level at parturition of 9.50 mg/100 ml. The average preinfusion serum calcium of the calves was 9.86 mg/100 ml. After infusion serum calcium was 9.65 mg/100 ml, and it

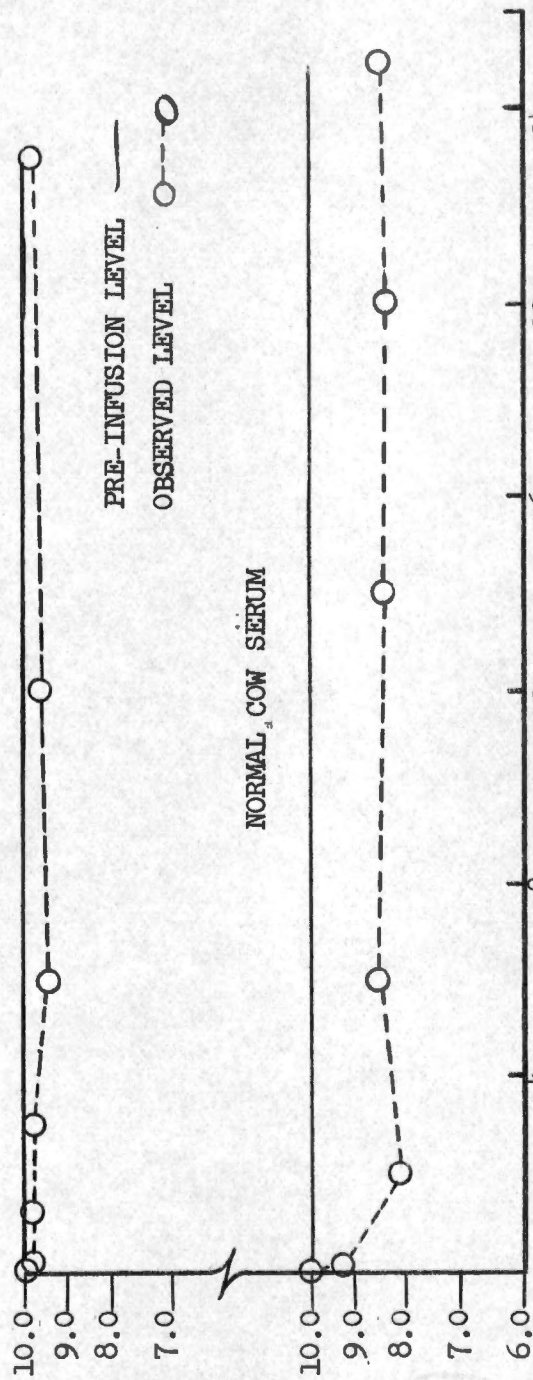

Figure 7. Average serum calcium response of two normal calves to intravenous infusion of parturient serum from a normal and a thyroid-damaged cow.

fluctuated between 9.4 and 9.8 mg/100 ml for the remainder of the trial.

Normal thyroid function appeared to be required for the hypocalcemic effect. The total amount of thyroxine infused with the control serum was insignificant. Therefore, the failure of thyroid-damaged cow serum to lower normal blood calcium levels may be ascribed, primarily, to the lack of circulating calcitonin. Although rat and human sera rapidly inactivate porcine calcitonin (167), and homologous calcitonin is cleared rapidly from the blood of pigs (175) and rabbits (94), there is no evidence that similar events occur in bovine serum. The prolonged effect observed in the calves indicated that either no inactivation was occurring or that some other factor was responsible for the decrease. Ochs and associates (131) noted the same kind of effect in their study. However, Nurimo (130) could not demonstrate hypocalcemic activity in serum from cows with milk fever.

Although the results of the two experiments should be considered cautiously due to the small numbers involved, they indicate that calcitonin may have an important role in the calcium metabolism of cows at parturition.

II. ROLE OF THE THYROID IN THE NORMAL CALCIUM METABOLISM OF CATTLE

A. Effects of Thyroid Damage on Calcium Metabolism in Growing Calves

Experiment 6. The results of this experiment are shown in Figures 8 and 9 and Tables 3, 4, 5, and 6. The calcium, phosphorus, and magnesium content of the hay and grain fed, were 6.16, 3.00, and 2.76 mg per g (mg/g) for the hay and 5.22, 3.57, and 1.71 mg/g for the grain. The calcium to phosphorus ratio of the diet consumed by the thyroid-damaged group was 1.71 ± 0.01. The corresponding value for the diet consumed by

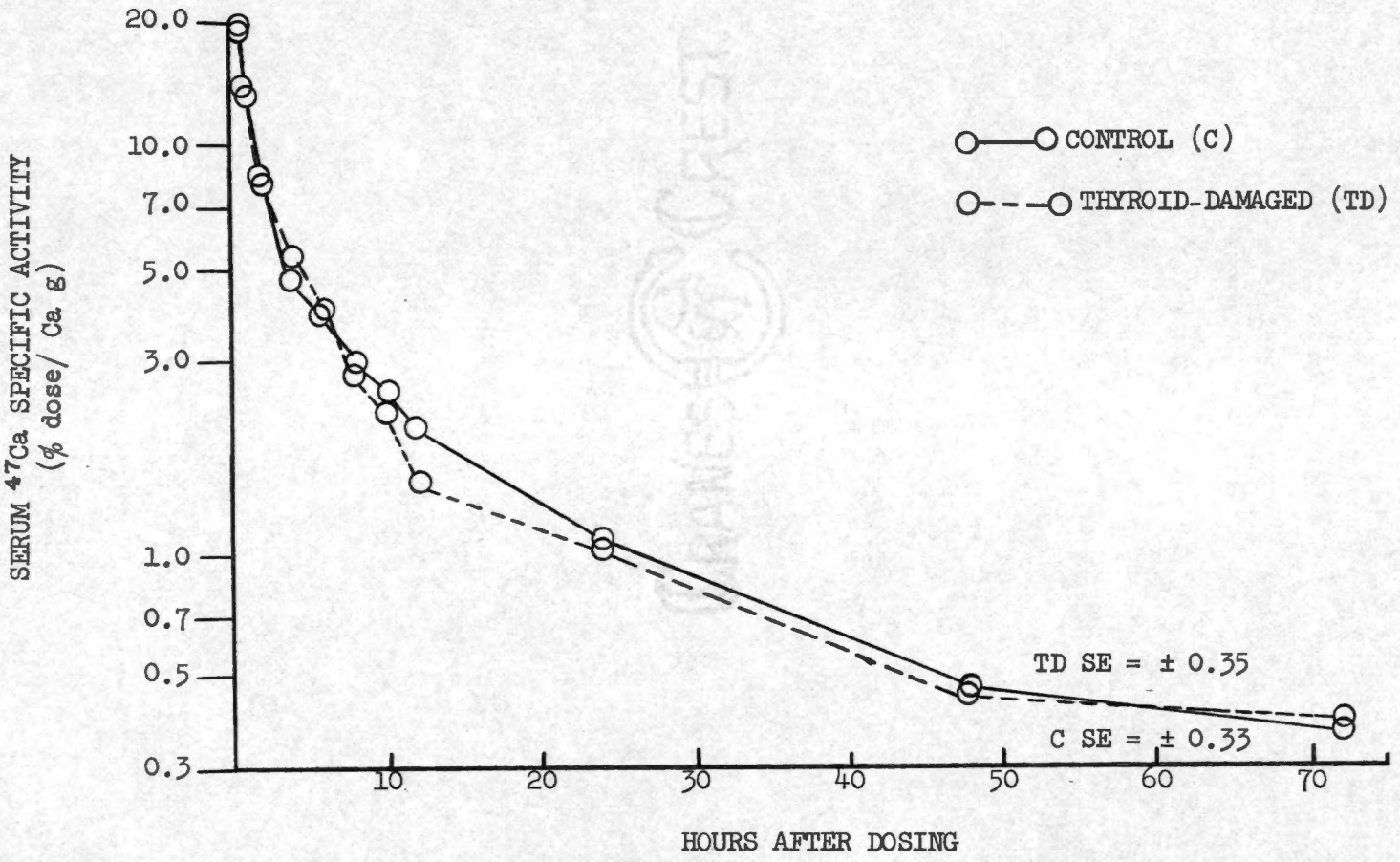

Figure 8. Average serum ^{47}Ca specific activity of three thyroid-damaged and three control calves used in Experiment 6 over the first 72 hours after intravenous dosing.

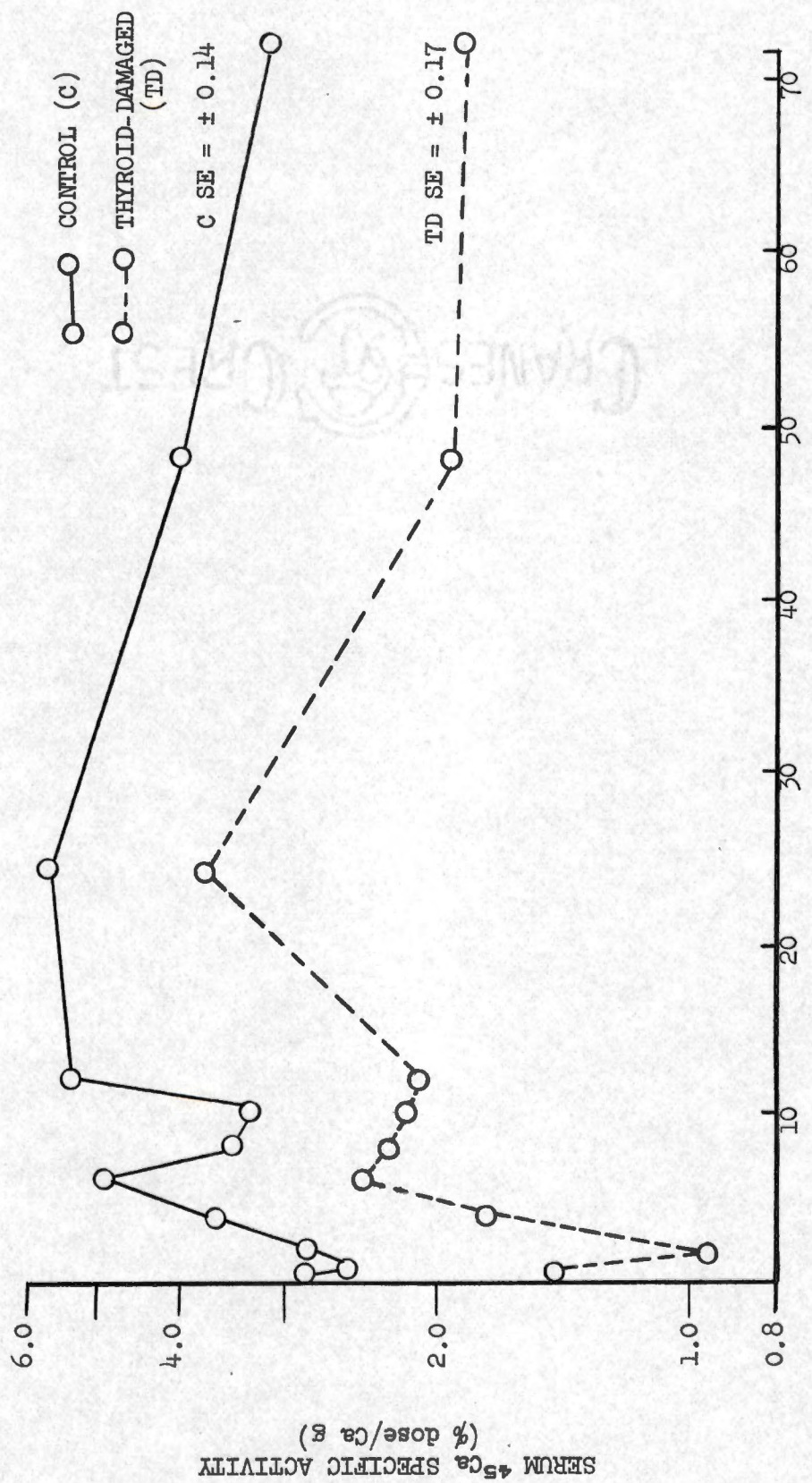

Figure 9. Average serum ^{45}Ca specific activity of three thyroid-damaged and three control calves used in Experiment 6 over the first 72 hours after oral dosing.

TABLE 3. Some measures of thyroid function in thyroid-damaged and control calves used in Experiment 6

Calf	Treatment	Protein bound iodine	Thyroxine	^{125}I uptake 120 hours
		——μg/100 ml serum——		% dose
110	Thyroid-damaged	1.2	0.44	0.24
111	Thyroid-damaged	2.9	0.64	3.57
112	Thyroid-damaged	2.2	0.52	2.54
561	Control	7.1	5.91	21.30
562	Control	8.5	5.82	30.82
563	Control	6.7	5.46	40.34
Avg	Thyroid-damaged[1]	2.10 ± 0.49	0.53 ± 0.06	2.12 ± 0.98
Avg	Control[1]	7.43 ± 0.55	5.73 ± 0.14	30.82 ± 5.49

[1]Mean ± SE.

TABLE 4. Daily intake, excretion, and balance[1] data for thyroid-damaged and control calves fed hay and grain in Experiment 6[2]

Identity	Thyroid-damaged	Control
Total feed intake (g)[3]	3693.8 ± 77.6	2271.0 ± 90.4
Total DM intake (g)[3]	3227.8 ± 68.0	1982.1 ± 79.2
DM digestibility (%)[3]	66.20 ± 1.05	72.87 ± 1.04
Daily intake[3]		
Calcium (g)[3]	20.93 ± 0.46	12.48 ± 0.50
Phosphorus (g)[3]	12.19 ± 0.25	7.73 ± 0.31
Magnesium (g)[3]	8.15 ± 0.19	4.58 ± 0.19
Daily fecal calcium (g)[3]	18.40 ± 1.37	7.52 ± 0.55
Daily urinary calcium (g)[3]	0.14 ± 0.02	0.09 ± 0.01
Daily fecal phosphorus (g)[3]	10.91 ± 0.78	6.24 ± 0.42
Daily urinary phosphorus (g)[3]	0.34 ± 0.07	1.17 ± 0.11
Daily fecal magnesium (g)[3]	5.81 ± 0.36	3.07 ± 0.21
Daily urinary magnesium (g)[3]	2.05 ± 0.13	1.07 ± 0.08
Daily balance		
Calcium (g)	+ 2.13 ± 0.67	+ 4.68 ± 0.49
Phosphorus (g)	+ 0.94 ± 0.18	+ 0.33 ± 0.11
Magnesium (g)	+ 0.34 ± 0.05	+ 0.50 ± 0.12

[1]Balance period 5 days.

[2]Each value is the mean of three calves per treatment ± SE.

[3]Means significantly different ($P < .05$).

TABLE 5. Intake, excretion, and balance data[1], expressed per kg body weight, for the thyroid-damaged and control calves fed hay and grain in Experiment 6[2]

Identity	Thyroid-damaged	Control
Total feed intake (g/kg)	269 ± 7	242 ± 15
Total DM intake (g/kg)	235 ± 6	211 ± 13
Daily intake		
Calcium (g/kg)[3,4]	0.152 ± 0.000	0.133 ± 0.000
Phosphorus (g/kg)[4]	0.088 ± 0.000	0.083 ± 0.002
Magnesium (g/kg)[3,4]	0.059 ± 0.000	0.049 ± 0.000
Daily fecal calcium (g/kg)[3,4]	0.135 ± 0.000	0.085 ± 0.000
Daily urinary calcium (mg/kg)	1.14 ± 0.08	1.09 ± 0.25
Daily fecal phosphorus (g/kg)	0.080 ± 0.001	0.067 ± 0.007
Daily urinary phosphorus (mg/kg)[3]	2.40 ± 0.89	12.31 ± 2.09
Daily fecal magnesium (g/kg)	0.042 ± 0.001	0.033 ± 0.004
Daily urinary magnesium (mg/kg)	15.00 ± 1.91	10.80 ± 1.33
Daily balance		
Calcium (mg/kg)[3]	+ 17.30 ± 5.41	+ 46.98 ± 5.94
Phosphorus (mg/kg)	+ 6.88 ± 1.48	+ 3.49 ± 1.12
Magnesium (mg/kg)[3]	+ 2.46 ± 0.34	+ 5.29 ± 1.05

[1]Balance period 5 days.

[2]Each value is the mean of three calves per treatment ± SE.

[3]Means significantly different ($P < .05$).

[4]SE < 0.000 not reported.

TABLE 6. Radiocalcium balance[1] data for thyroid-damaged and control calves dosed simultaneously with ^{47}Ca intravenously and ^{45}Ca orally in Experiment 6[2]

Identity	Thyroid-damaged		Control	
	^{47}Ca	^{45}Ca	^{47}Ca	^{45}Ca
Fecal excretion				
(% dose)	12.92 ± 2.11	35.29 ± 3.22	6.38 ± 0.94	26.17 ± 2.07
(% dose/kg BW)	0.097 ± 0.020	0.27 ± 0.02	0.067 ± 0.008	0.28 ± 0.02
Urinary excretion				
(% dose)	0.47 ± 0.14	0.95 ± 0.10	0.29 ± 0.002	0.71 ± 0.05
(% dose/kg BW)	0.003 ± 0.001	0.007 ± 0.001	0.003 ± 0.001	0.007 ± 0.000[3]
Digestive tract recovery				
(% dose)	Negligible	1.92 ± 0.41	Negligible	1.41 ± 0.30

[1]Balance period 5 days.

[2]Each value is the mean of three calves per treatment ± SE.

[3]SE < 0.000 not reported.

controls was 1.62 ± 0.02. Table 3 shows the extent of damage in the thyroid-damaged calves. Thyroid destruction was not complete but circulating thyroxine levels were very low.

Since the groups differed an average of 44 kg in body weight, the data summarized in Table 4 have been recalculated on a per kg of body weight basis and summarized in Table 5. The large differences in feed and dry matter intake evident in Table 4 were due to size differences. However, thyroid-damaged calves had slightly greater feed and dry matter intakes per kg body weight. The increased digestibility of the control diet was due to a decrease in the hay to grain ratio of the diet consumed by that group. Percentage of total dry matter intake which came from grain was 69.27 in the control group but only 54.13 in the thyroid-damaged group. The daily intake of calcium, phosphorus, and magnesium was related to body weight through the latters' effect on feed intake. There was less difference between groups on a per kg of body weight basis than when the total intakes were compared. However, some differences were still apparent. When corrected for body weight differences, the difference in fecal calcium excretion between treatments was reduced. This was due to decreased feed intake differences. There were no treatment effects on urinary excretion of calcium.

The fecal excretion of phosphorus per kg of body weight was not significantly different between treatments whereas the total quantities excreted were different. This was due to decreased intake differences. The urinary excretion of phosphorus was significantly greater in controls than in thyroid-damaged animals. Significant ($P < .05$) differences in fecal magnesium were abolished by correcting for body weight differences. Urinary magnesium difference was also decreased. As a result of lower

fecal losses, calcium balance was twice as high in controls as in thyroid-damaged calves. Phosphorus balance was small and positive. The higher balance in the thyroid-damaged group was due to decreased urinary phosphorus excretion. Magnesium balances did not differ significantly between groups. Per kg of body weight, controls retained significantly more calcium and magnesium as a result of decreased excretion. Calcium, phosphorus, and magnesium intakes were well above NRC recommendations (125).

Total fecal excretions of oral and intravenous radiocalcium, Table 6, page 72, were not significantly greater in thyroid-damaged animals than in controls. Correction for body weight differences reduced the apparent difference in excretion of oral or intravenous radiocalcium. The reason was that feed intake per unit body weight was almost equal in the two groups. Since fecal output is related to intake, it would be related to body size. Radiocalcium in the digestive tract of large animals would be mixed with a greater volume of ingesta and excreted in the feces. Faster rate of passage in animals consuming more feed could also be a factor. The findings of Van't Klooster (171) that high roughage rations bind more calcium per unit weight than low roughage rations was not substantiated. The apparent differences between groups in urinary radiocalcium excretion were abolished by expressing the results per kg of body weight. Radiocalcium concentrations were not different between groups. Therefore, urinary volume must have been proportional to size. There were no differences in digestive tract retention of radiocalcium between groups.

There was no significant difference in average serum calcium of the groups throughout the trial, 10.62 ± 0.14 mg/100 ml for the thyroid-damaged vs 10.39 ± 0.11 mg/100 ml for the control group. Phosphorus

levels of thyroid-damaged calves averaged 5.69 ± 0.10 mg/100 ml whereas controls averaged only 4.97 ± 0.10 mg/100 ml, a significant difference ($P < .05$). This finding could have been a reflection of decreased urinary phosphorus excretion of the thyroid-damaged group. Average magnesium levels of thyroid-damaged and control calves were 2.96 ± 0.06 and 2.74 ± 0.07 mg/100 ml. This difference was nonsignificant ($P > .05$).

Average serum ^{47}Ca and ^{45}Ca specific activities of thyroid-damaged and control groups are shown in Figure 8, page 67, and Figure 9, page 68. There was no significant difference in ^{47}Ca specific activity. This agrees with work reported in the literature (137). Average serum ^{45}Ca specific activity of thyroid-damaged calves was significantly lower ($P < .05$) than controls throughout the trial. Others (137) have reported decreased serum radiocalcium levels after oral dosing in hypothyroid animals.

Endogenous fecal loss of calcium of the two groups was not significantly different (Table 7). There was no difference in true absorption or retention of ^{45}Ca. The true digestibility of dietary calcium was higher in controls than in thyroid-damaged animals but this difference was not statistically significant ($P > .05$). A 15% increase in the dietary intake of calcium from an inorganic source resulted in an average 300% increase in digestibility. This is much greater than the increase found by Hansard and associates (68) when inorganic calcium supplements replaced hay. However, true digestibility and endogenous losses are lower than those given by Hansard and associates (67) for cattle of similar age. There was no difference between groups in the size of the "available calcium" pool, but turnover of the pool was faster in controls than in thyroid-damaged calves. However, the difference was not significant

TABLE 7. Estimates[1] of calcium metabolism parameters in thyroid-damaged and control calves dosed simultaneously with ^{47}Ca intravenously and ^{45}Ca orally in Experiment 6[2]

Identity	Thyroid-damaged	Control
Fecal endogenous calcium (g)	1.60 ± 0.15	1.22 ± 0.21
Fecal endogenous calcium (mg/kg BW)	11.70 ± 1.26	12.93 ± 1.95
True absorption of radiocalcium (%)	74.54 ± 5.25	79.95 ± 2.50
% oral ^{45}Ca retained	73.59 ± 5.29	79.23 ± 2.50
% of absorbed ^{45}Ca retained	98.72 ± 0.20	99.10 ± 0.07
True digestibility of dietary calcium (%)	17.99 ± 13.09	46.01 ± 5.91
"Available calcium" pool (g)	44.58 ± 5.56	33.54 ± 5.30
"Available calcium" pool 1/2 time (hrs)	20.27 ± 1.32	17.08 ± 0.66
% dose in rib		
Intravenous ^{47}Ca	0.47 ± 0.004	0.40 ± 0.01
Oral ^{45}Ca	0.31 ± 0.02	0.37 ± 0.03
% dose in femur		
Intravenous ^{47}Ca	3.67 ± 0.13	3.84 ± 0.12
Oral ^{45}Ca[3]	2.44 ± 0.10	3.64 ± 0.17

[1]Based on a balance period of 5 days.

[2]Each value is the mean of three calves per treatment ± SE.

[3]Means significantly different ($P < .05$).

($P > .05$). Bone uptake of ^{47}Ca was not different between groups. In contrast, ^{45}Ca bone uptake was depressed in thyroid-damaged calves.

Low ^{45}Ca specific activity in the thyroid-damaged calves as compared to controls, Figure 9, page 68, could not be due to increased blood clearance because the turnover rate of calcium was slower than in controls. Although bone uptake of ^{45}Ca was less in thyroid-damaged calves, ^{47}Ca uptake was not different between groups. There was no difference between groups in endogenous loss or urinary excretion of calcium.

Apparently absorption was defective. The large average difference in true digestibility coupled with the small absolute difference in dry matter digestibility indicated a defect in absorption of calcium. Significantly, the lack of difference in true absorption was due to abnormally high absorption in one animal of the thyroid-damaged group. The ^{47}Ca fecal loss of this calf was 57% of the oral ^{45}Ca fecal loss. The average of the other calves was about 33%. An error in analysis was suspected, but could not be confirmed.

The major findings in this experiment were: strong indications of a decreased absorption of calcium in thyroid-damaged animals which could account for the lower calcium balances in these animals compared to controls; a significantly lower serum phosphorus in thyroid-damaged calves than controls; and indications of a decreased turnover of body calcium in the thyroid-damaged calves compared to controls, as shown by the calcium pool half-times.

Experiment 7. The results of this experiment are summarized in Figures 10 and 11, and Tables 8, 9, and 10. Thyroid damage was not extremely severe in one of the thyroid-damaged animals, Table 8. Also,

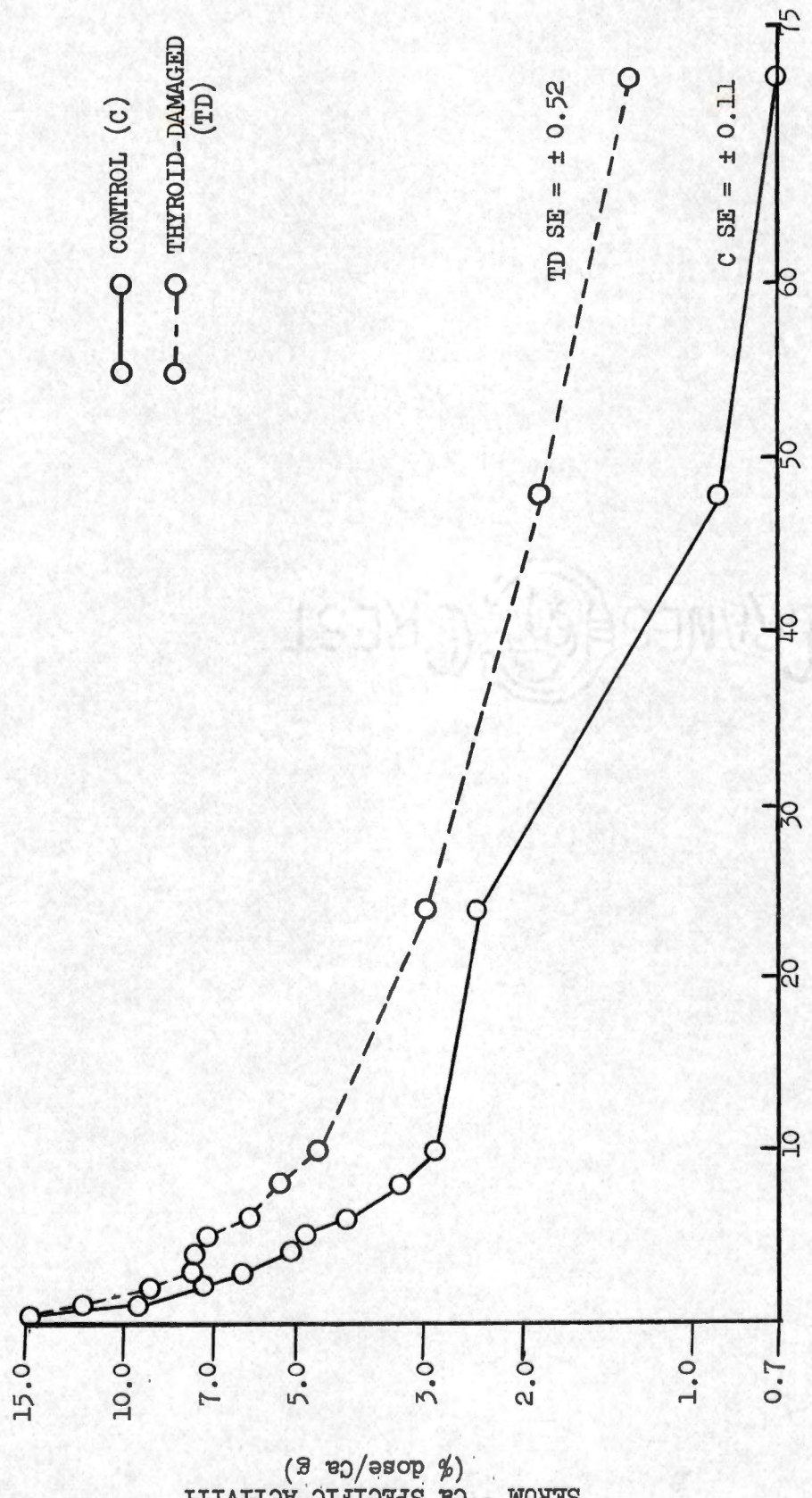

Figure 10. Average serum ^{47}Ca specific activity of two thyroid-damaged and two control calves used in Experiment 7 over the first 72 hours after intravenous dosing.

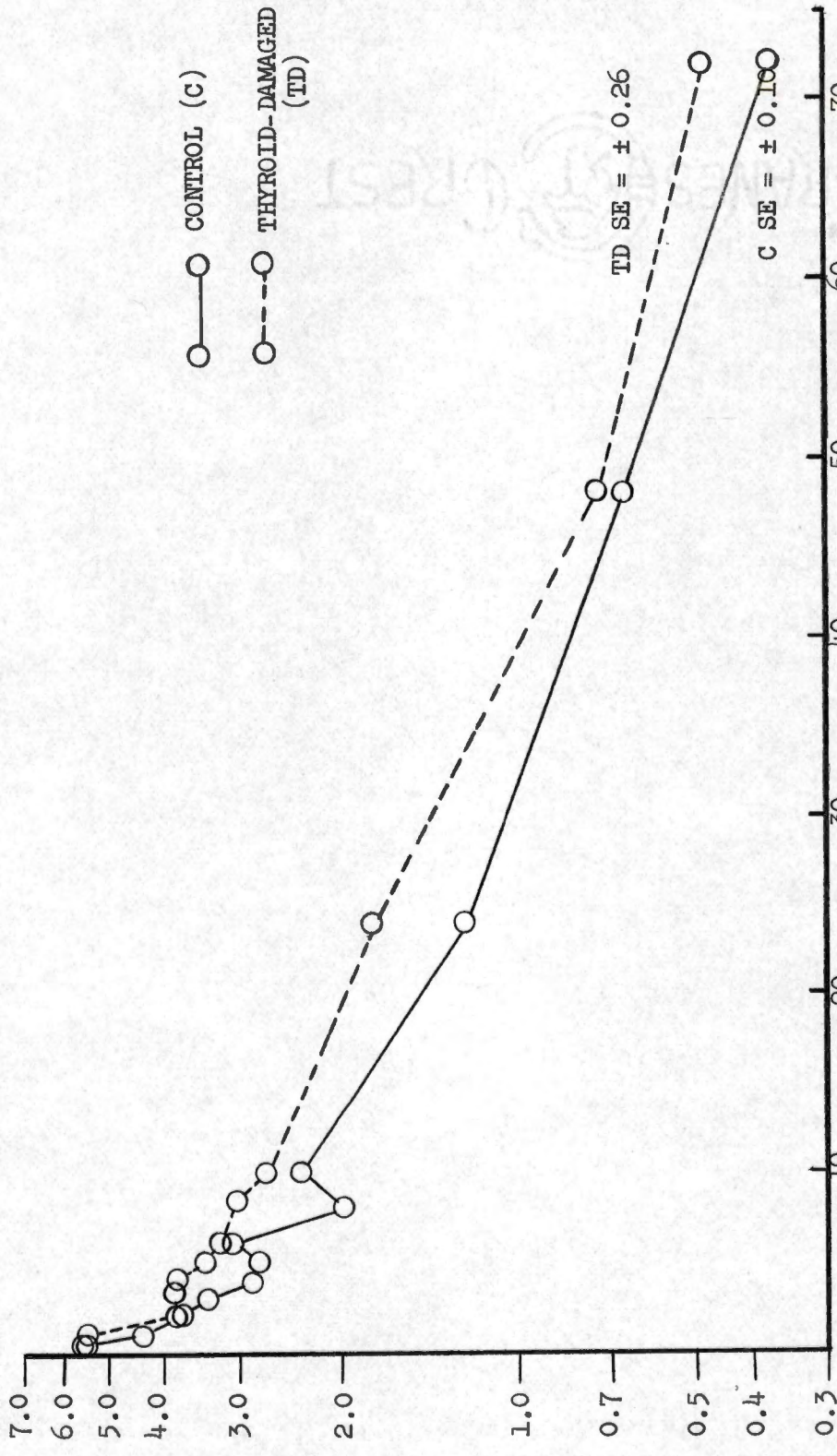

Figure 11. Average serum ^{45}Ca specific activity of two thyroid-damaged and two control calves used in Experiment 7 over the first 72 hours after oral dosing.

TABLE 8. Some measures of thyroid function on thyroid-damaged and control calves used in Experiment 7

Calf	Treatment	Protein bound iodine	Thyroxine	^{125}I uptake 144 hrs
		——μg/100 ml serum——		% dose
121	Thyroid-damaged	2.9	---[2]	4.96
251	Thyroid-damaged	0.6	0.44	0.22
253	Control	7.2	10.60	15.17
271	Control	7.0	10.03	13.46
Avg	Thyroid-damaged[1]	1.75 ± 1.15	---	2.59 ± 2.37
Avg	Control[1]	7.10 ± 0.10	10.31 ± 0.29	14.32 ± 0.86

[1]Mean ± SE.

[2]Sample not analyzed.

TABLE 9. Intake, excretion, and balance[1] data for thyroid-damaged and control calves fed hay and grain in Experiment 7[2]

Identity	Thyroid-damaged	Control
Total food intake (g)	3615 ± 355	3983 ± 63
Total DM intake (g)	3255 ± 321	3585 ± 57
DM digestibility (%)	74.52 ± 2.11	71.13 ± 1.73
Daily intake		
Calcium (g)	22.58 ± 2.32	24.80 ± 0.43
Phosphorus (g)	11.69 ± 1.05	12.95 ± 0.17
Magnesium (g)	7.40 ± 0.93	8.01 ± 0.20
Daily fecal calcium (g)	16.55 ± 2.26	23.40 ± 1.87
Daily urinary calcium (g)	0.26 ± 0.03	0.24 ± 0.04
Daily fecal phosphorus (g)	7.82 ± 0.85	9.12 ± 0.65
Daily urinary phosphorus (g)	0.23 ± 0.07	0.21 ± 0.05
Daily fecal magnesium (g)	4.96 ± 0.59	7.55 ± 0.53
Daily urinary magnesium (g)	1.55 ± 0.23	1.22 ± 0.13
Daily balance		
Calcium (g)	+ 5.77 ± 1.71	+ 1.72 ± 2.00
Phosphorus (g)	+ 3.64 ± 0.74	+ 3.63 ± 0.69
Magnesium (g)	- 0.68 ± 0.66	- 2.55 ± 0.68

[1]Balance period 5 days.

[2]Each value is the mean of two calves per treatment ± SE.

TABLE 10. Radiocalcium balance[1] data for thyroid-damaged and control calves dosed simultaneously with ^{47}Ca intravenously and ^{45}Ca orally in Experiment 7[2]

Identity	Thyroid-damaged		Controls	
	^{47}Ca	^{45}Ca	^{47}Ca	^{45}Ca
Fecal excretion (% dose)	17.57 ± 0.56	48.16 ± 4.04	14.51 ± 3.13	60.52 ± 0.18
Urinary excretion (% dose)	2.92 ± 0.32	0.97 ± 0.34	2.70 ± 0.22	0.84 ± 0.02
Digestive tract recovery (% dose)	Negligible	9.32 ± 1.94	Negligible	6.06 ± 0.03

[1]Balance period 5 days.

[2]Each value is the mean of two calves per treatment ± SE.

when compared to the other controls used in these experiments, these controls were hyperthyroid.

The calcium, phosphorus, and magnesium levels of the hay and grain were 6.38, 2.66, and 3.13, and 5.63, 3.84, and 0.90 mg/g respectively. The calcium to phosphorus ratios of the diets consumed by the thyroid-damaged and control calves averaged 1.91 ± 0.03 and 1.84 ± 0.07. Table 9 shows that there was no difference in feed intake or dry matter intake and digestibility. Intakes of calcium, phosphorus, and magnesium were not different between groups and were sufficient to meet requirements. Control calves lost more calcium in feces than thyroid-damaged calves but urinary excretion was the same for both groups. No difference in phosphorus excretion was noted. Control calves lost more magnesium in feces than thyroid-damaged calves. As a result of the greater fecal calcium and magnesium losses, controls had less positive calcium and magnesium balances than thyroid-damaged calves. Magnesium balances were slightly negative in both groups. None of the comparisons were significantly different ($P > .05$). The calcium infused did not have significant effects on calcium balance. The balances were on the same order as those in Experiment 6. Phosphorus balance was higher in this experiment than in Experiment 6.

There was no difference in ^{47}Ca excretion in feces and urine between groups, Table 10. Although urinary excretion of ^{45}Ca was not different between groups, controls excreted more ^{45}Ca in the feces than did thyroid-damaged calves. The difference was not statistically significant. The reason for the larger excretions of ^{45}Ca, especially in controls, in this experiment than in Experiment 6 was not apparent. There was no evidence of scours during the balance trial. The higher urinary loss of both oral

and intravenous radiocalcium was the result of fecal contamination. Increased urinary loss of stable calcium over Experiment 6 values also indicated that contamination had occurred. More ^{45}Ca was recovered from the digestive tract of thyroid-damaged animals than from controls.

Serum calcium was not consistently different between groups. As in Experiment 6, serum phosphorus in thyroid-damaged calves was consistently higher than in controls. The difference, however, was not statistically significant ($P > .05$). There was no difference in serum magnesium. Figure 10, page 78, shows a consistently but not significantly slower clearance of ^{47}Ca from blood in thyroid-damaged calves than in controls. Both groups cleared calcium from the blood more slowly than the calves in Experiment 6. Initial serum ^{47}Ca specific activity levels were approximately the same in the two experiments.

On the basis of the results of Experiment 6 and reports in the literature (161, 173), it was expected that the highest serum ^{45}Ca levels would be noticed 12 to 24 hours after dosing. The atypical shape of the oral ^{45}Ca serum specific activity curves, Figure 11, page 79, can not be explained satisfactorily. If the dose had bypassed the rumen and gone to the abomasum, an early maximum serum calcium specific activity might be expected. Calcium is absorbed from the abomasum (42) at a rapid rate (31). The rapid recycling of large amounts of radiocalcium in saliva, as reported by Hansard and associates (66), could account for the finding that no difference in the excretion pattern of oral radiocalcium between the calves of this experiment and the calves in Experiment 6 existed. The atypical pattern has been seen in some unreported data. Controls cleared ^{45}Ca at a slightly faster rate than did thyroid-damaged calves, but the differences were not statistically significant ($P > .05$).

As in Experiment 6, there was no difference between groups in endogenous fecal calcium loss, Table 11. The true absorption of oral radiocalcium was higher in thyroid-damaged calves than controls. This difference was not significant. Absorption in these damaged calves was about 10% below the values reported in Experiment 6. Control absorption was 30% lower than values reported in the preceding experiment. There was no difference in retention of absorbed radiocalcium. The true digestibility of dietary calcium in controls was 17% of Experiment 6 levels. The thyroid-damaged calves digested about 80% more calcium in this experiment than the damaged calves in Experiment 6. However this difference was not significant ($P > .05$). In contrast, dry matter digestibility, Table 9, page 81, in the thyroid-damaged and control groups was the same. These findings indicated that a defect in absorption of calcium existed in controls. The size of the "available calcium" pool was not significantly different between groups but the turnover rate was significantly slower ($P < .05$) in thyroid-damaged calves than in controls. There was no difference between groups in either ^{47}Ca or ^{45}Ca uptake of bones. However, as a result of low absorption, ^{45}Ca uptake was low.

The slower blood clearance of ^{47}Ca in thyroid-damaged calves, Figure 10, page 78, was due to slower calcium turnover. The slower disappearance of ^{45}Ca from blood in thyroid-damaged calves, Figure 11, page 79, was due to both slower turnover rate and higher absorption than in controls. In view of the large differences in absorption and significant differences in turnover rates, the differences in serum ^{45}Ca specific activity of the groups should have been greater. This anomaly can not be explained from the data at hand.

TABLE 11. Estimates[1] of calcium metabolism parameters in thyroid-damaged and control calves dosed simultaneously with ^{47}Ca intravenously and ^{45}Ca orally in Experiment 7[2]

Identity	Thyroid-damaged	Control
Fecal endogenous calcium (g)	1.56 ± 0.27	1.50 ± 0.51
True absorption of radiocalcium (%)	62.86 ± 4.47	46.23 ± 1.48
% oral ^{45}Ca retained	61.89 ± 4.14	45.40 ± 1.48
% absorbed ^{45}Ca retained	98.49 ± 0.41	98.21 ± 0.01
True digestibility of dietary calcium (%)	26.35 ± 11.85	7.75 ± 5.72
"Available calcium" pool (g)	21.32 ± 5.50	27.42 ± 1.65
"Available calcium" pool 1/2 time (hrs)[3]	40.54 ± 1.39	26.16 ± 0.61
% dose in rib		
Intravenous ^{47}Ca	0.87 ± 0.24	0.52 ± 0.36
Oral ^{45}Ca	0.22 ± 0.03	0.21 ± 0.03
% dose in femur		
Intravenous ^{47}Ca	4.72 ± 1.29	2.79 ± 1.76
Oral ^{45}Ca	1.61 ± 0.19	1.20 ± 0.20

[1]Based on a balance period of 5 days.

[2]Each value is the mean of two calves per treatment ± SE.

[3]Means differ significantly ($P < .05$).

The defect in calcium absorption may have been due to the effects of hyperthyroidism in controls. These calves had circulating thyroxine levels, Table 8, page 80, greater than those of thyroid-damaged calves fed 30 mg l-thyroxine daily. Several workers have reported that hyperthyroidism decreased absorption of calcium (57, 128, 132, 164). At any rate, the major findings in this experiment were: an apparent decreased absorption of calcium in controls, due perhaps to excessive endogenous thyroxine; consistently but not significantly greater serum phosphorus levels of thyroid-damaged calves than in controls; and significantly slower ($P < .05$) turnover of the "available calcium" pool in thyroid-damaged calves than in controls.

Experiment 8. Results of this experiment are shown in Figures 12 and 13, and in Tables 12, 13, 14, and 15. Table 12 shows that the thyroxine therapy was excessive. Circulating thyroxine levels were three times that of normal calves and two times as high as calves on oral thyroxine therapy. Thus, the thyroid-damaged calves were hyperthyroid instead of euthyroid.

The calcium, phosphorus, and magnesium contents of the hay and grain fed in Part 2 of the experiment were 7.53, 2.64, and 2.55 mg/g for the hay and 5.63, 3.84, and 0.90 mg/g for the grain. The calcium to phosphorus ratio of the diet consumed by thyroid-damaged calves was 2.07 ± 0.01. For the controls the ratio was 2.06 ± 0.01. In Part 3 of the experiment grain composition was the same as for Part 2. Hay in Part 3 contained 6.83, 2.66, and 3.13 mg/g of calcium, phosphorus, and magnesium. The calcium to phosphorus ratios of diets consumed by the damaged and control calves were 1.97 ± 0.01 and 1.97 ± 0.01.

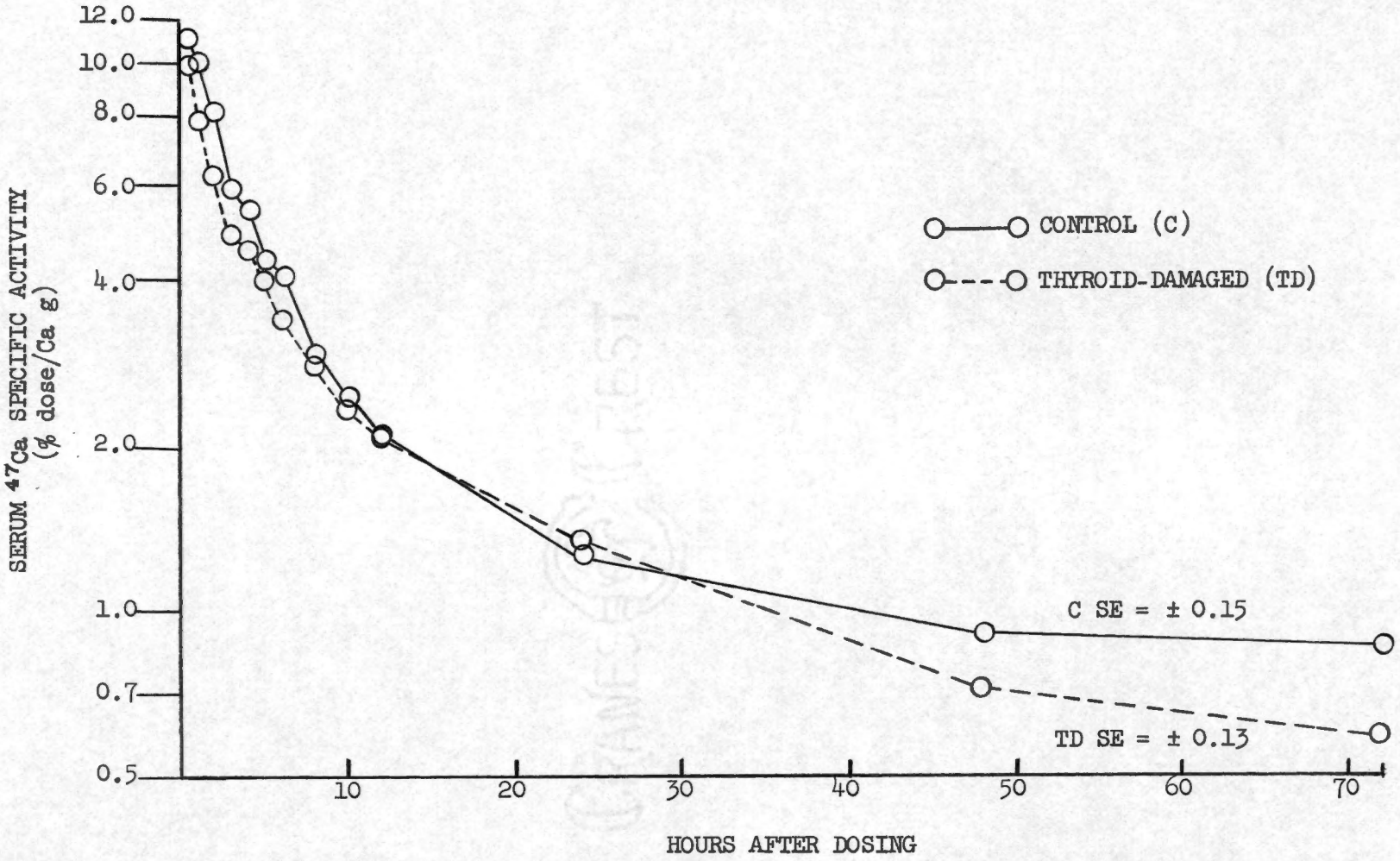

Figure 12. Average serum ^{47}Ca specific activity of three thyroxine supplemented thyroid-damaged and three unsupplemented control calves used in Experiment 8 over the first 72 hours after intravenous dosing.

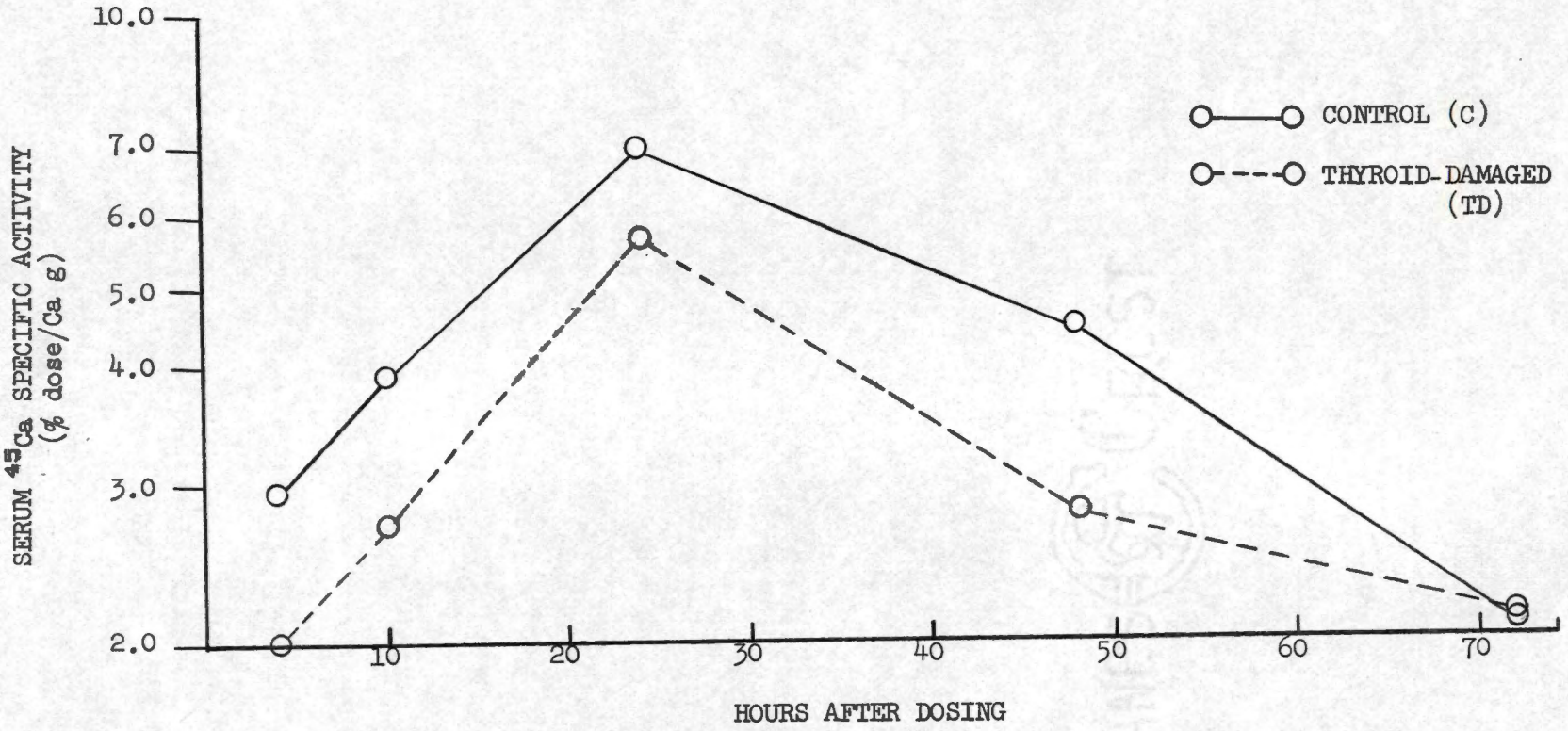

Figure 13. Average serum ^{45}Ca specific activity of three thyroxine supplemented thyroid-damaged and three unsupplemented control calves used in Experiment 8 over the first 72 hours after oral dosing.

TABLE 12. Some measures of thyroid function in thyroxine supplemented[1] thyroid-damaged, and control calves used in Parts 2 and 3 of Experiment 8

Calf	Treatment	Protein bound iodine	Thyroxine	^{125}I uptake 120 hrs
		μg/100 ml serum		% dose
119	Thyroid-damaged	17.1	24.68	0.06
120	Thyroid-damaged	16.9	18.71	0.26
124	Thyroid-damaged	15.1	18.97	0.11
252	Control	5.4	6.24	10.23
564	Control	3.6	5.72	13.64
565	Control	7.6	5.39	11.39
Avg	Thyroid-damaged[2]	16.37 ± 0.64	20.79 ± 1.95	0.14 ± 0.06
Avg	Control[2]	5.53 ± 1.16	5.78 ± 0.25	11.75 ± 1.00

[1]Thyroid-damaged calves received 3 mg l-thyroxine subcutaneously daily.

[2]Mean ± SE.

TABLE 13. Intake, excretion, and balance[1] data for thyroid-damaged[2] and control calves fed hay and grain in Part 2 of Experiment 8[3]

Identity	Thyroid-damaged	Control
Total feed intake (g)	4271 ± 47	4147 ± 63
Total DM intake (g)	3886 ± 43	3770 ± 58
DM digestibility (%)	65.89 ± 0.91	63.76 ± 0.77
Daily intake		
Calcium (g)	28.36 ± 0.35	27.40 ± 0.48
Phosphorus (g)	13.68 ± 0.12	13.35 ± 0.17
Magnesium (g)	7.59 ± 0.12	7.27 ± 0.16
Daily fecal calcium (g)	19.91 ± 1.59	20.09 ± 1.44
Daily urinary calcium (g)	0.13 ± 0.02	0.09 ± 0.01
Daily fecal phosphorus (g)	13.14 ± 0.80	13.19 ± 0.69
Daily urinary phosphorus (g)	0.62 ± 0.04	0.43 ± 0.06
Daily fecal magnesium (g)	6.56 ± 0.45	7.66 ± 0.57
Daily urinary magnesium (g)	2.28 ± 0.18	2.11 ± 0.12
Daily balance		
Calcium (g)	+ 8.32 ± 1.42	+ 7.24 ± 1.43
Phosphorus (g)	- 0.08 ± 0.76	- 0.27 ± 0.60
Magnesium (g)	- 1.16 ± 0.49	- 2.49 ± 0.53

[1]Balance period 5 days.

[2]Thyroid-damaged calves received 3 mg l-thyroxine subcutaneously daily.

[3]Each value is the mean of three calves per treatment ± SE.

TABLE 14. Intake, excretion, and balance[1] data for thyroid-damaged[2] and control calves fed hay and grain in Part 3 of Experiment 8[3]

Identity	Thyroid-damaged	Control
Total feed intake (g)	4396 ± 4	4390 ± 10
Total DM intake (g)	3998 ± 4	3993 ± 20
DM digestibility (%)	65.75 ± 0.85	64.84 ± 1.11
Daily intake		
Calcium (g)	27.62 ± 0.03	27.58 ± 0.07
Phosphorus (g)	14.05 ± 0.01	14.03 ± 0.03
Magnesium (g)	9.30 ± 0.01	9.28 ± 0.03
Daily fecal calcium (g)	19.61 ± 0.66	17.26 ± 0.84
Daily urinary calcium (g)	0.15 ± 0.02	0.16 ± 0.03
Daily fecal phosphorus (g)	7.48 ± 0.32	7.73 ± 0.49
Daily urinary phosphorus (g)	0.11 ± 0.01	0.07 ± 0.01
Daily fecal magnesium (g)	6.45 ± 0.26	6.32 ± 1.16
Daily urinary magnesium (g)	2.15 ± 0.25	2.18 ± 0.24
Daily balance		
Calcium (g)	+ 7.83 ± 0.67	+ 10.16 ± 0.87
Phosphorus (g)	+ 6.46 ± 0.32	+ 6.27 ± 0.50
Magnesium (g)	+ 0.70 ± 0.44	+ 0.78 ± 0.45

[1]Balance period 5 days.

[2]Thyroid-damaged calves received 3 mg l-thyroxine subcutaneously daily.

[3]Each value is the mean of three calves per treatment ± SE.

TABLE 15. Radiocalcium balance[1] data for thyroid-damaged[2] and control calves dosed with ^{47}Ca intravenously in Part 2 and ^{45}Ca orally in Part 3 of Experiment 8[3]

Identity	Thyroid-damaged		Controls	
	^{47}Ca	^{45}Ca	^{47}Ca	^{45}Ca
Fecal excretion (% dose)	9.03 ± 1.08	38.01 ± 2.50	9.41 ± 0.94	35.48 ± 1.66
Urinary excretion (% dose)	0.72 ± 0.09	1.39 ± 0.24	0.80 ± 0.07	1.71 ± 0.32
Digestive tract recovery (% dose)	---	4.81 ± 0.41	---	5.92 ± 3.25

[1]Balance period 5 days.

[2]Thyroid-damaged calves received 3 mg l-thyroxine subcutaneously daily.

[3]Each value is the mean of three calves per treatment ± SE.

Table 13 contains the results of the balance during Part 2 of the experiment. No significant differences in feed intake, dry matter intake, or dry matter digestibility were observed. There was no significant difference in intake of calcium, phosphorus, magnesium or calcium and phosphorus excretion between treatments. Slightly less magnesium was lost in thyroid-damaged calves than in controls but the differences were not significant ($P > .05$). As a result magnesium balances were slightly less negative in thyroid-damaged calves than controls. There was no significant difference in daily calcium or phosphorus balance. Table 14 contains the results of the balance during Part 3 of the experiment. There were no significant differences between groups in intake measurements. The intakes of calcium and phosphorus for the balance periods did not differ significantly. Magnesium intake was significantly ($P < .05$) higher in Part 3 than in Part 2 of the experiment. Less calcium was excreted in the feces of controls during Part 3 than during Part 2. More calcium was lost in the thyroid-damaged group than in controls in the third part of the experiment, but neither difference was significant ($P > .05$). Significantly less ($P < .05$) phosphorus was excreted by both groups in Part 3 than in Part 2 of the experiment. Magnesium excretion was not different between groups in Part 3 and no significant difference in magnesium excretion between trials was noted. In Part 3, lower fecal excretion of calcium by thyroid-damaged calves than controls resulted in more positive calcium balances. The difference was not significant. Neither phosphorus nor magnesium balances differed significantly between groups, but both balances were more positive than in Part 2. Calcium, phosphorus, and magnesium intakes in both balances were sufficient to meet requirements.

No significant differences in the fecal or urinary excretion of oral or intravenous radiocalcium due to treatment were noted, Table 15, page 93. Fecal losses were similar to those of thyroid-damaged calves in Experiment 6. Digestive tract retention of oral ^{45}Ca was not significantly different between groups.

Figure 12, page 88, shows that the thyroid-damaged calves cleared ^{47}Ca from blood slightly faster than controls over the first 12 hours after injection. The same relationship was evident in later hours. The differences were not significant ($P > .05$). Much the same result occurred in the case of ^{45}Ca, Figure 13, page 89. There were no significant differences between groups during the trial. There was no consistent difference in serum calcium between the two groups during Part 2 of the experiment. No consistent difference in phosphorus or magnesium levels was noted. In Part 3, there was no significant difference in serum calcium, phosphorus, or magnesium between groups.

Endogenous fecal calcium loss was not significantly lower for thyroid-damaged calves than controls, Table 16. Endogenous losses in both groups were lower than in Experiments 6 and 7. True absorption was not significantly different. Retention of ^{45}Ca, true digestibility, and "available calcium" pool size were not significantly different between groups. The pool half-time was shorter in thyroid-damaged calves than controls, but the difference was not significant. The opposite was true in Experiments 6 and 7. No estimates of bone radiocalcium uptake were made.

Since absorption and true digestibility did not differ greatly, the lower serum ^{45}Ca specific activity, Figure 13, of the thyroid-damaged group was probably due to increased blood calcium turnover, as indicated

TABLE 16. Estimates[1] of calcium metabolism parameters in thyroid-damaged[2] and control calves dosed with ^{47}Ca intravenously in Part 2, and ^{45}Ca orally in Part 3 of Experiment 8[3]

Identity	Thyroid-damaged	Control
Fecal endogenous calcium (g)	0.76 ± 0.04	1.08 ± 0.14
True absorption of calcium (%)	68.18 ± 3.03	71.25 ± 2.08
% oral ^{45}Ca retained	66.77 ± 3.15	69.55 ± 2.21
% absorbed ^{45}Ca retained	97.90 ± 0.39	97.58 ± 0.48
True digestibility of dietary calcium (%)	27.14 ± 6.69	31.04 ± 1.56
"Available calcium" pool (g)	36.70 ± 5.41	41.83 ± 4.73
"Available calcium" pool 1/2 time (hrs)	25.15 ± 3.22	32.90 ± 3.43

[1]Based on a balance period of 5 days.

[2]Thyroid-damaged calves received 3 mg l-thyroxine subcutaneously daily.

[3]Each value is the mean of three calves per treatment ± SE.

by the shorter pool half-time, in the thyroid-damaged group. This increased turnover was stimulated by hyperthyroidism. Several workers (12, 13, 106, 137) reported hyperthyroidism increased body calcium mobility.

The results of Experiment 6 indicated that a defect in absorption of calcium was present in thyroid-damaged calves. In Experiment 7 the low calcium absorption in controls, due perhaps to hyperthyroidism, could have masked defects in absorption of calcium in the thyroid-damaged calves. Experiment 8 showed that high levels of thyroxine did not affect absorption of calcium from the digestive tract. These contradictory findings concerning thyroxine effects on calcium absorption cannot be resolved with the data at hand. Alternatively, the difference could be due to a thyroxine potentiated mechanism which was not present in the thyroid-damaged calves. Calcitonin has not been shown to affect gut absorption of calcium (45), but secretion of calcitonin at normal serum calcium levels has been reported (61, 90). In all three experiments the level of thyroxine affected body calcium turnover. The higher serum phosphorus levels in thyroid-damaged than control calves found in Experiments 6 and 7 were not evident in Experiment 8 in the prethyroxine period, Figure 6, page 56.

The small number of calves and the variability of the results make definite statements tenuous. One point that can be made is that thyroid-damaged calves appeared to have a defect in calcium absorption which was not evident if the damaged calves were given thyroxine. A more important conclusion may be that thyroxine affects the turnover rate of body calcium. Since serum calcium was not changed, the increased resorption was counterbalanced by accretion and excretion.

Significantly, the finding of increased body calcium turnover in hyperthyroidism supports the explanation that the treatment differences illustrated in Figure 5, page 55, and Figure 6, page 56, were partially or entirely due to effects of thyroxine on bone resorption and accretion.

B. Effects of Thyroid Status and Thyroxine Therapy on Calcium Metabolism in Lactating Cows

Experiment 9. The results of this experiment are shown in Table 17. In the first trial the percentage of the intravenous radiocalcium dose lost daily in milk and the average milk to plasma ratio were significantly ($P < .05$) higher for the normal than for the thyroid-damaged cow. This was the result of both higher milk yield and greater concentration in the normal cow. Although milk production and the daily loss of radiocalcium in milk did not differ significantly in the two trials, the milk to plasma ratio difference between cows seen in trial 1 was not evident in trial 2. This was due to a decreased milk to plasma ratio in the normal cow. The injection of thyroid stimulating hormone decreased the milk to plasma ratio in the normal cow by stimulating thyroxine secretion. Increased thyroxine levels increased mobilization of calcium from body stores, which effect diluted the radiocalcium available with stable calcium and lowered the milk to plasma ratio.

Experiment 10. The results of this experiment are shown in Figures 14 and 15 and Table 18. When supplemental thyroxine was given, there was no difference between the milk to plasma ratios of the thyroid-damaged cow and her controls, Table 18. Without thyroxine therapy the milk to plasma ratio of the thyroid-damaged cow was significantly ($P < .05$) greater

TABLE 17. Effects of injection of thyroid stimulating hormone (TSH) on the utilization of intravenously administered radiocalcium in lactating athyroid and control cows[1]

Identity	Without TSH		With TSH[3]	
	Thyroid-damaged	Control	Thyroid-damaged	Control
Milk yield (kg/day)	4.53 ± 0.06	8.95 ± 0.37	4.27 ± 0.26	10.09 ± 0.89
Milk radiocalcium (% dose/day)	4.46 ± 1.96	15.11 ± 9.09	4.55 ± 1.92	9.17 ± 5.26
% dose/l milk	0.99 ----	1.69 ----	1.07 ----	0.91 ----
Milk:plasma ratio of ^{47}Ca	13.43 ± 2.16	26.86 ± 4.05	11.34 ± 1.80	11.25 ± 1.74
Cumulative fecal excretion[2]	21.48 ----	26.83 ----	23.61 ----	21.59 ----

[1]Each value is mean ± SE.

[2]Balance period 5 days.

[3]1 mg partially purified TSH given intravenously for 5 successive milkings.

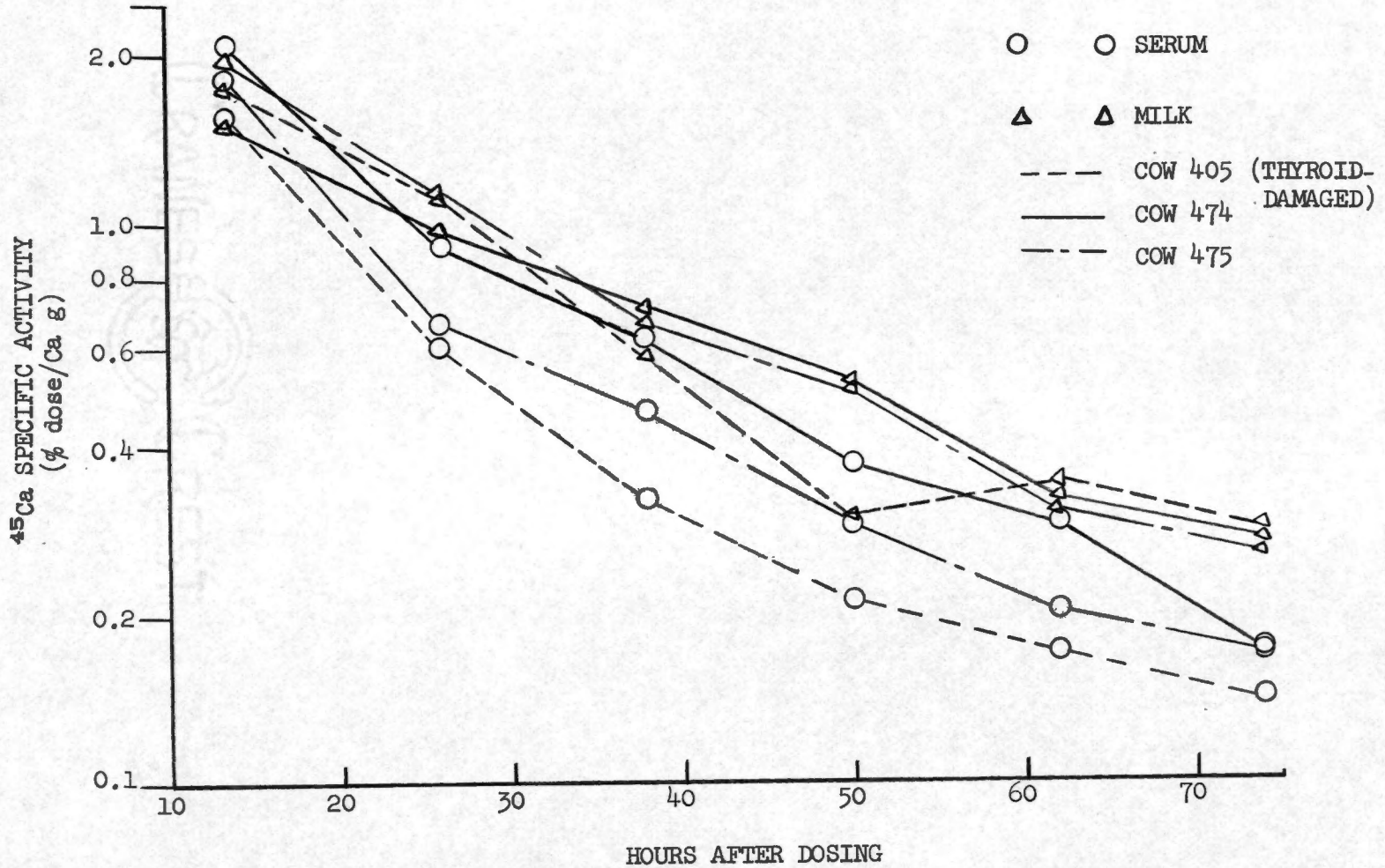

Figure 14. Serum and milk ^{45}Ca specific activity of a thyroxine supplemented thyroid-damaged cow and two controls over the first 75 hours after intravenous dosing.

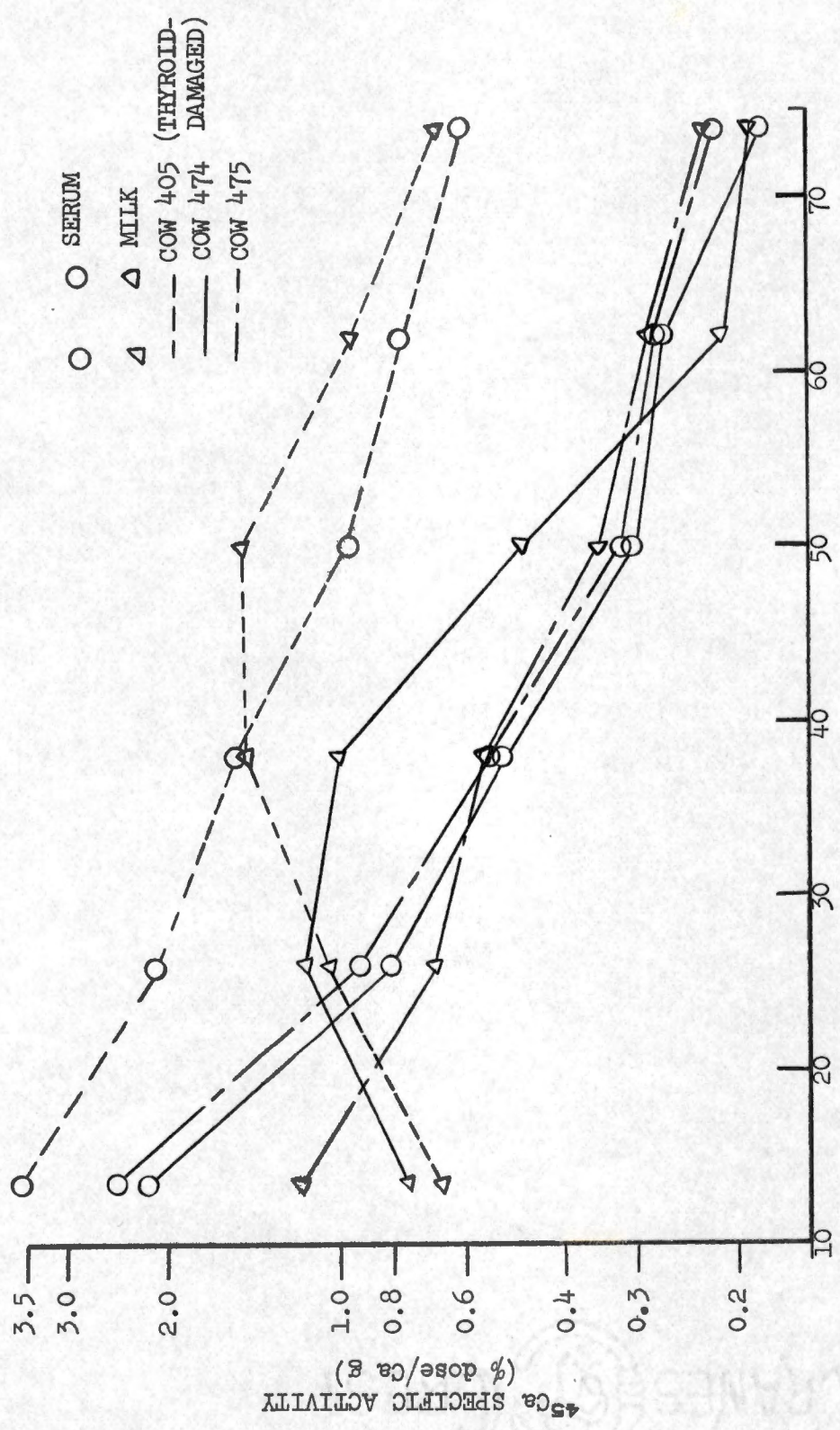

Figure 15. Serum and milk ^{45}Ca specific activity of a thyroid-damaged cow and two controls over the first 75 hours after intravenous dosing.

TABLE 18. Effects of altering thyroid status on the utilization of intravenously administered radiocalcium in a lactating thyroid-damaged cow and two controls[1]

Identity	Thyroid-damaged	Control	Control
		With thyroxine therapy[2]	
Milk yield (kg/day)	14.54 ± 0.25	8.94 ± 0.67	10.95 ± 0.30
Milk radiocalcium (% dose/day)	7.18 ± 3.88	3.70 ± 1.46	5.30 ± 2.61
Milk:plasma ratio of ^{45}Ca	13.16 ± 1.99	11.36 ± 1.66	12.66 ± 1.56
Milk calcium (g/day)	16.55 ± 0.53	10.47 ± 0.65	12.90 ± 0.34
Endogenous fecal calcium (g/day)	8.24 ± 2.50	9.11 ± 0.51	6.51 ± 0.24
		Without thyroxine therapy	
Milk yield (kg/day)	1.31 ± 0.22	8.95 ± 0.18	8.04 ± 0.33
Milk radiocalcium (% dose/day)	2.16 ± 0.43	4.85 ± 1.76	3.68 ± 1.70
Milk:plasma ratio of ^{45}Ca	17.39 ± 3.86	13.04 ± 1.73	11.10 ± 0.92
Milk calcium (g/day)	1.88 ± 0.39	10.72 ± 1.12	9.22 ± 0.71
Endogenous fecal calcium (g/day)	2.15 ± 0.63	5.76 ± 0.86	8.90 ± 2.72

[1]Values are mean ± SE.

[2]5 mg l-thyroxine subcutaneously daily to thyroid-damaged cow.

than the average of her controls. During thyroxine therapy the daily milk production of the thyroid-damaged cow was significantly greater ($P < .05$) than that of controls, but the reverse was true when thyroxine therapy was not given. There was no significant difference in the daily loss of radiocalcium in milk between trials. This could account, in part, for the change in milk to plasma ratio. Moreover, the low milk yield of the thyroid-damaged cow in the second trial was associated with an increase in the calcium concentration of the milk of 0.25 mg calcium per ml. Although this difference was not significant ($P > .05$), it dictates caution in assessing the meaning of the milk to plasma ratio changes. In Figure 14 it is shown that there were no apparent differences between cows in serum and milk specific activity in the first trial. The values plotted are the average of two successive samples. The corresponding time is the half time between samples. Figure 15 shows that in the second trial serum and milk calcium specific activity were definitely higher in the thyroid-damaged cow than her controls. This was due primarily to a significantly ($P < .05$) decreased excretion of stable calcium by the thyroid-damaged cow (Table 18). Also endogenous fecal loss in the thyroid-damaged cow was significantly decreased ($P < .05$) in the second trial. No consistent decreases occurred in the controls. These results indicated that supplemental thyroxine increased the mobilization of body calcium and, therefore, turnover of body calcium.

These two diverse experiments indicated that the factor responsible for the observed results was the thyroxine stimulated mobilization of body calcium reserves. Interpretation of results must be qualified due to the small number of animals used. Also, it is not possible to determine the significance of the extremely high milk to plasma ratio of the control cow in the first trial of Experiment 9.

C. Placental Transfer of Calcium in Thyroid-damaged and Normal Cattle

Three control cows transferred an average of 34.92 ± 4.13% of their dose to their calves during an average of 10 days after dosing. Three thyroid-damaged cows transferred an average of 38.90 ± 3.36% of their dose to their calves during an average of 14 days after dosing. This difference was not statistically significant. These values are higher than the 21.3% over a 7-day period reported by Hansard (64). The longer time interval may be partially responsible for this difference. Another reason could be that total analysis, as conducted here, eliminated sampling errors inherent in the earlier work. Small numbers of animals in both studies tend to limit the statistical stability of these results.

Summarizing discussion. Although the evidence obtained in the infusion studies described above is only circumstantial, no important role of calcitonin in the hypercalcemic response of cattle has been established. Calcitonin was reported to be required for the normal hypercalcemic response of rats (60, 77, 166), rabbits (94), dogs (40), pigs (29), humans (63, 114, 148), sheep (28, 139), and goats (56). Calcitonin is present in cattle (20) and bovine thyroid parafollicular cells hypertrophy in response to prolonged hypercalcemia (25). However normal circulating calcitonin levels are very low (98), and calcitonin injections 50 to 100 times the normal level are required to elicit a decrease in serum calcium (139, 93). Hypercalcemia sufficient to induce a profound increase in calcitonin secretion in sheep (139) produced only slight responses in calves. These results indicated that a major role of calcitonin in the response of cattle to hypercalcemia was improbable.

The important role of thyroxine in the response of cattle to hypercemia indicated by the results agrees with the work of Jowsey and Detenbeck (83) who found that in dogs calcitonin did not lower serum calcium in the absence of normal thyroxine levels. Moreover, restoring normal thyroxine levels in thyroidectomized dogs restored the normal ability to counteract hypercalcemia. Milhaud (114) noted that calcitonin administered to hypercalcemic patients was ineffective unless adequate thyroxine levels were present. Similarily Riggs and associates (148) reported that thyroxine therapy almost completely restored the ability of hypothyroid patients to counteract hypercalcemia. Also, thyroxine therapy of thyroidectomized rats restored 50% of the normal ability to counteract hypercalcemia (60), and iodine deficients rats could not counteract hypercalcemia as well as controls (122). Thus thyroxine appears to be involved in the hypercalcemic response of several species.

The finding that the thyroid was required for the "normal" serum calcium depression seen at parturition lends support to the suggestion of Capen and Young (24) that large releases of calcitonin at parturition could be a factor in the etiology of milk fever. Increased circulating calcitonin levels in cows with milk fever (98) are further support for this theory. Several factors argue against such a simple explanation. First, contrary to results of the present experiments and of Ochs et al. (131), Nurimo (130) could not demonstrate hypocalcemic activity in serum from cows with milk fever. Second, cows with milk fever cleared intravenously injected calcium as fast as controls (1, 43). Third, mastectomy removed 80% of the "normal" drop in serum calcium at parturition. Fourth, there is no clear evidence that bone resorption, the only established site of calcitonin action, is altered in cattle at parturition (14, 73, 110, 130, 135, 152).

In the second group of experiments, the consistent finding that the level of circulating thyroxine affected the turnover of body calcium is in agreement with the reports of Blaxter (13) in sheep and Blaxter (12) and Owen (132) in cattle which showed that hyperthyroidism increased the turnover of bone calcium and calcium loss from the body. Payne and associates (137) found that injections of thyroxine increased the rate of bone accretion and exchangeable calcium pool size in thyroparathyroidectomized goats. Hyperthyroidism increased accretion rates to above normal levels. In humans, the weight of clinical evidence (2, 81, 83, 91, 114) is consistent with the theory that thyroxine affects the rate and extent of bone accretion and resorption; and studies with rats showing that hyperthyroidism resulted in depletion of calcitonin from thyroids (176) and decreased bone formation (57), support the same conclusion. In dogs (21) thyroidectomy was followed by almost complete cessation of both accretion and resorption. Parathyroid status had no effect on the response. Also Adams and Jowsey (3) reported that hyperthyroidism in dogs caused increased accretion and resorption. The parathyroid was not required for the effects on resorption. Their conclusion that thyroxine directly affected the mineral exchanges of bone is in agreement with the findings of the present experiments.

In the present experiments the findings concerning thyroxine effects on calcium absorption are conflicting. Lowered absorption in a group of unsupplemented thyroid-damaged calves is in accord with the results of Care and associates (30) who reported that thyroparathyroidectomy of sheep decreased the absorption of calcium and the conclusion of Levin (99) that thyroidectomy decreased the absorption of calcium from the small intestine of the rat. Payne and others (137) noted that absorption

of calcium was decreased in thyroparathyroidectomized goats. However, according to Gittes and Irvin (60) Aub and associates found increased net absorption of calcium in hypothyroid humans. Jowsey and Detenbeck (83) reported that Lowe et al. found absorption to be increased in hypothyroid patients. Thyroxine therapy decreased absorption to normal levels.

The low calcium absorption in intact hyperthyroid calves seen in the present studies is in agreement with the results of Blaxter (12, 13) and Owen (132) who concluded that excess thyroxine decreased net calcium absorption in sheep and cattle and work with rats by Friedland and associates (57) and Noble and Matty (128) who showed the same was true in that species. However, hyperthyroidism did not affect calcium absorption in thyroid-damaged calves. In this connection Payne et al. (137) noted that thyroxine therapy increased absorption of calcium to normal levels in thyroparathyroidectomized goats. The anomalous effects of hyperthyroidism on calcium absorption cannot be resolved with the information at hand.

CHAPTER V

SUMMARY AND CONCLUSIONS

Eleven experiments were conducted using a total of 27 cows and 25 calves to determine the role of the thyroid gland in calcium metabolism in the bovine.

The purpose of the first three experiments was to determine the role of calcitonin in the response of cattle to hypercalcemia induced by intravenous infusion of calcium solutions. The critical assumption in these three experiments was that ^{131}I thyroid damage had destroyed or damaged the source of calcitonin. In the first experiment three athyroid and three normal cattle were used. A slower clearance of calcium in the athyroid cattle than controls 2 to 8 hours after infusion was apparent but not statisticaly significant. Since the difference was not apparent in the first 2 hours, when calcitonin secretion should have been maximally stimulated, a simple calcitonin deficiency may not have been the sole cause. However, controls cleared calcium from the blood significantly faster during the first 4 hours after infusion than athyroid cattle. In the second experiment iodinated casein fed thyroid-damaged cows cleared calcium from blood as well as controls. There were no treatment differences in serum magnesium or phosphorus. Phosphorus levels of both groups fell after infusion and remained low. Thyroid-damaged cows cleared calcium faster than controls during the first 4 hours, the period when calcitonin release would be highest in controls. Adequate thyroxine therapy restored normal ability to counteract hypercalcemia. Alternatively, a defect may not have been present in the thyroid-damaged cows used in the second experiment.

The third experiment utilized three normal, three radioiodine thyroid-damaged, and three surgically thyroidectomized calves. The damaged calves were receiving thyroxine therapy which was actually excessive. Consequently, they were slightly hyperthyroid. When account was taken of differences in initial serum calcium levels, no consistent treatment effects on calcium clearance were noted. No calcitonin defect was evident. The possibility exists that no defect in hypercalcemic response was present in the damaged calves but this is doubtful.

The results of these experiments indicated that the defect in calcium clearance seen in the athyroid cattle in the first experiment was remedied by thyroxine replacement therapy. Supplemental thyroxine could act directly on bone turnover. However, if an extrathyroidal source of calcitonin was present, and if thyroxine was required for calcitonin action, the results expected would be similar to those observed. The homeostatic defect of the athyroid cattle in the first experiment appeared to be more complex than a simple calcitonin deficiency.

Three other calcium infusion studies were performed. Three thyroid-damaged and three control calves were made hypercalcemic before and during thyroxine therapy to the thyroid-damaged calves. When account was taken of differences between groups in preinfusion serum calcium, there was no difference in the clearance of calcium between unsupplemented thyroid-damaged calves and controls. After therapy, there appeared to be a defect in the response of thyroid-damaged calves to hypercalcemia. This was the result of hyperthyroidism in the damaged calves due to excessive thyroxine therapy. No consistent differences in serum phosphorus and magnesium were noted. In another trial, although their serum calcium levels were higher, thyroid-damaged calves cleared calcium at a faster

rate than controls. This could have been due to a combination of excess thyroxine present in the controls and a deficiency of calcitonin in the damaged calves. Serum phosphorus of the thyroid-damaged calves was consistently higher than controls, but no effect of thyroid status on serum magnesium was evident.

Assuming calcitonin secretion was actually defective in the thyroid-damaged animals used in these experiments, the results did not clearly demonstrate a major role of calcitonin in the hypercalcemic response of cattle. However, the evidence is only circumstantial. A definite role of thyroxine could be inferred from the data.

To determine if calcitonin might be involved in the calcium metabolism of cows at parturition, two experiments were conducted. In the first experiment, serum calcium, phosphorus, and magnesium were determined one week prior to calving, at calving, and one week after calving in six pairs of thyroid-damaged and normal cattle. Since serum calcium did not decrease in parturient thyroid-damaged cows, calcitonin appeared to be required for the drop in serum calcium seen at parturition in controls. No effect of thyroid status on serum phosphorus was evident. Serum magnesium levels rose on the day of calving. This effect was independent of thyroid status. In the second experiment, serum from a normal and a thyroid-damaged parturient cow was infused into young calves. Serum calcium of the calves was depressed when infusion of normal parturient cow serum was given. No such effect was evident when serum from the thyroid-damaged cow was given. These results could be attributed, with reservation, to higher calcitonin levels in the serum of the normal cow. The results of these two experiments indicated that calcitonin was important in calcium metabolism of cows at parturition. Thyroxine did not appear to be involved.

Six other experiments were conducted to study the role of the thyroid gland in the normal calcium metabolism of cattle. In three experiments a total of eight thyroid-damaged and eight normal calves received simultaneous oral ^{45}Ca and intravenous ^{47}Ca doses. Concurrent 5-day chemical and radiochemical balances were conducted. Digestive tract contents and representative bones were taken at slaughter and analyzed.

In the first experiment there appeared to be a defect in absorption of calcium in the three thyroid-damaged calves. The turnover of body calcium was also slower than in the three controls. Serum phosphorus of thyroid-damaged calves was significantly higher ($P < .05$) than that of controls but calcium and magnesium were not different. In the second experiment, hyperthyroidism in the two controls may have decreased absorption of calcium, which effect masked possible defects in absorption of calcium in the two thyroid-damaged animals. Body calcium turnover was significantly slower in the thyroid-damaged calves than controls. Serum phosphorus of thyroid-damaged calves was consistently higher than that of controls. In the third experiment, three thyroid-damaged calves receiving excessive thyroxine therapy, absorbed as much calcium as three controls. Turnover of body calcium was more rapid in the hyperthyroid calves than in controls. Serum phosphorus, calcium, and magnesium differences, with or without thyroxine therapy were not apparent. These experiments indicated that the turnover of body calcium was related to level of circulating thyroxine. There appeared to be a defect in calcium absorption in thyroid-damaged calves that was eliminated by thyroxine therapy. Seemingly opposite effects of hyperthyroidism on calcium absorption in control and thyroid-damaged calves could not be explained with the data at hand.

Two experiments were conducted with lactating cows to determine the effects of altered thyroxine status on calcium utilization for milk production. In one experiment partially purified thyrotrophin, acting through increased thyroxine secretion, stimulated increased body calcium turnover in the control but not in the athyroid cow. In the other experiment, cessation of thyroxine therapy to a thyroid-damaged cow was followed by decreased mobilization of body stores for milk production. Both experiments indicated that thyroxine affected mobilization of body calcium.

Results of an experiment with three pairs of thyroid-damaged and normal cows indicated that thyroid damage did not affect the transfer of calcium from the dam to the fetus.

Although no clear role for calcitonin in the hypercalcemic response of cattle could be demonstrated, interactions of calcitonin and thyroxine could, theoretically, explain many of the observed results. Calcitonin appeared to be involved in the drop in serum calcium at parturition. Thyroxine exerted its effects on calcium metabolism by affecting body calcium turnover. There appeared to be a defect in absorption of calcium in thyroid-damaged calves that was eliminated when adequate or excessive thyroxine therapy was given.

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APPENDIX

TABLE 19. Individual serum calcium and magnesium concentration of cows used in Experiment 1

Hours	Thyroid-damaged 209	Thyroid-damaged 292	Thyroid-damaged 821	Control 385	Control 389	Control 822
	(mg/100 ml)					
	Calcium					
-2	11.0	10.5	9.4	10.6	10.5	10.5
-1	9.9	9.9	8.5	9.5	10.4	10.3
0	10.3	10.2	8.8	11.2	9.4	9.1
1	17.5	16.9	16.3	17.3	16.5	15.4
2	14.4	14.5	11.4	15.0	14.6	13.3
3	13.9	13.4	11.8	13.4	11.0	11.4
4	13.2	12.5	10.5	11.7	11.0	10.5
5	12.2	12.2	11.7	11.7	10.4	10.8
6	11.9	12.0	11.2	10.8	10.2	11.3
7	11.9	11.3	11.5	9.9	10.3	10.8
8	10.5	10.5	11.0	9.0	11.0	11.0
12	10.3	9.7	10.0	10.8	11.0	10.5
16	10.3	9.3	9.4	10.5	10.3	12.2
20	10.3	9.5	9.4	9.9	11.0	11.5
24	10.0	9.7	9.6	10.1	11.0	11.2
	Magnesium					
-2	2.28	2.63	1.97	1.82	2.08	2.08
-1	2.25	2.26	1.92	1.92	1.98	2.04
0	1.98	2.19	1.87	1.81	1.98	1.89
1	3.51	3.67	3.46	2.77	3.06	2.89
2	2.84	2.97	2.04	2.04	2.21	2.29
3	2.43	2.40	1.68	1.66	1.65	1.69
4	2.60	2.57	2.44	1.72	1.85	1.85
5	2.45	2.30	2.26	1.58	1.72	1.72
6	2.37	2.20	2.04	1.54	1.71	1.68
7	2.45	2.32	2.26	1.76	2.10	2.01
8	2.52	2.29	2.38	1.94	2.18	2.05
12	2.48	2.34	1.94	1.69	1.92	1.86
16	2.63	2.40	1.94	1.92	1.99	2.02
20	2.56	2.47	1.77	1.90	1.93	1.94
24	2.49	2.46	1.72	1.87	1.82	1.89

TABLE 20. Individual serum calcium and magnesium concentration of cows used in Experiment 2

Hours	Thyroid-damaged					Control				
	470	405	465	467	472	471	406	464	466	473
	(mg/100 ml)									
	Calcium									
-2	10.6	11.6	11.9	9.9	9.5	10.7	11.0	12.8	10.0	9.6
-1	9.9	10.8	10.6	10.1	9.6	10.5	9.5	12.1	10.4	10.2
0	10.4	10.8	10.6	10.2	9.1	11.0	10.6	11.9	10.1	9.9
1	11.8	14.6	13.0	13.0	15.6	13.7	15.8	13.4	12.0	14.0
2	11.9	13.0	12.6	11.8	12.4	12.8	13.1	12.2	11.0	13.5
3	11.2	12.3	11.7	11.5	12.0	12.5	12.1	12.3	11.3	12.0
4	11.7	12.7	11.3	11.7	11.3	12.5	12.2	12.3	11.4	12.2
5	11.6	----	----	11.5	11.6	12.5	----	----	11.5	12.4
6	10.8	11.4	11.6	11.0	11.9	10.9	11.0	11.6	10.2	10.6
7	10.5	10.3	11.0	11.2	11.9	10.8	10.3	11.1	10.2	10.2
8	10.7	10.2	10.8	10.8	11.2	10.0	10.1	10.8	10.6	10.2
12	9.8	10.1	10.6	11.0	11.4	10.7	10.2	11.3	10.3	9.5
16	10.0	10.7	10.8	10.5	10.9	10.1	10.8	10.7	10.0	10.1
20	10.5	10.1	11.1	10.6	11.9	10.5	10.5	11.2	10.1	9.5
24	9.9	10.7	10.8	10.1	10.1	10.0	10.1	10.9	9.6	10.1
	Magnesium									
-2	2.60	2.60	3.10	2.20	2.70	2.80	2.40	2.80	2.60	2.20
-1	2.60	2.20	2.80	2.30	2.50	2.50	2.30	2.50	2.50	2.20
0	2.70	2.25	2.90	2.40	2.30	2.60	2.30	2.80	2.50	2.40
1	2.40	2.40	2.60	2.20	2.80	2.40	2.20	2.50	2.20	2.10
2	2.70	2.30	2.80	2.40	2.70	2.70	2.50	2.40	2.30	2.60
3	3.50	2.70	3.60	3.10	2.90	3.50	2.90	3.60	3.20	2.80
4	2.70	2.60	3.50	2.80	2.60	3.00	2.70	2.90	2.90	2.60
5	2.60	----	----	2.80	2.50	3.50	----	----	3.10	2.40
6	3.10	2.50	3.30	2.70	2.20	3.50	2.90	2.80	2.60	2.40
7	3.60	2.60	3.40	3.00	2.40	3.50	2.40	2.70	3.00	2.40
8	3.30	2.70	3.70	2.90	2.80	3.60	2.90	2.90	3.00	2.50
12	3.70	2.90	3.70	2.90	2.60	3.60	3.00	3.50	3.10	2.60
16	3.90	3.30	3.90	3.50	2.70	3.60	3.70	3.30	4.00	2.80
20	3.40	2.90	3.10	3.10	2.70	3.50	3.20	3.40	3.50	2.90
24	3.00	3.00	3.40	2.80	2.30	3.70	2.90	3.20	2.80	2.80

TABLE 21. Average serum phosphorus values of cows used in Experiment 2[1]

Hours	Thyroid-damaged	Control
	(mg/100 ml)	
-2	6.80	7.22
-1	6.91	7.20
0	6.70	6.82
1	7.10	6.90
2	5.73	5.89
3	4.70	4.93
4	4.18	4.60
5	4.59	4.45
6	4.68	4.84
7	4.40	4.40
8	4.51	4.50
12	4.77	4.84
16	5.10	4.90
20	4.80	4.56
24	4.17	4.86

[1]Individual values lost after means were calculated.

TABLE 22. Individual serum calcium, phosphorus, and magnesium concentration of calves used in Part 1 of Experiment 8[1]

Hour	Thyroid-damaged			Control		
	119	120	124	252	564	565
	(mg/100 ml)					
	Calcium					
0	9.9	10.7	9.5	9.2	9.2	9.5
0.5	12.0	12.2	12.0	11.1	11.4	11.7
1	11.9	11.6	11.3	10.3	10.6	10.4
2	10.5	11.4	10.4	10.1	9.5	10.1
3	9.7	10.6	10.1	9.5	8.9	9.0
4	9.5	10.1	9.7	8.7	8.6	9.2
5	10.0	10.6	9.6	8.9	10.5	10.2
6	10.8	11.0	9.8	11.2	11.0	10.2
8	10.5	9.9	9.5	9.8	11.0	9.1
10	10.2	10.0	10.4	9.3	10.6	8.6
24	10.3	10.3	9.8	8.8	9.7	9.7
	Phosphorus					
0	8.9	7.2	8.3	8.6	8.8	8.2
0.5	7.0	6.3	6.8	7.3	6.9	7.0
1	6.7	6.3	7.9	7.4	7.0	6.9
2	7.1	6.5	6.4	6.5	6.2	6.1
3	6.2	6.2	6.1	6.3	5.7	5.5
4	6.0	6.5	6.6	6.2	6.2	5.8
5	5.7	6.6	6.5	6.4	6.6	5.9
6	5.8	6.0	6.3	6.8	6.6	6.3
8	6.5	6.4	6.1	6.8	7.2	7.1
10	7.1	6.8	7.1	7.2	8.1	7.6
24	8.1	6.8	8.1	8.3	8.0	8.2
	Magnesium					
0	3.15	3.10	3.35	2.50	2.65	3.05
0.5	3.70	2.50	3.55	3.15	2.75	2.60
1	2.25	2.55	3.00	2.90	3.15	2.65
2	2.50	3.10	2.85	2.70	2.45	2.35
3	2.10	2.85	3.15	2.35	2.60	2.35
4	2.65	3.15	3.30	2.35	2.75	2.65
5	2.90	3.20	3.10	2.45	3.45	3.10
6	2.55	3.05	3.40	3.05	2.70	2.60
8	2.45	2.40	3.50	2.50	3.05	2.75
10	2.80	2.95	3.80	2.50	3.00	3.50
24	3.30	3.15	3.85	2.35	3.20	3.55

[1]First 24 hours after dosing.

TABLE 23. Individual serum calcium, phosphorus, and magnesium concentration of calves used in Experiment 7[1]

Hours	Thyroid-damaged		Control	
	121	251	253	271
	(mg/100 ml)			
	Calcium			
0	11.3	10.9	11.5	10.8
0.5	14.7	14.9	13.2	12.0
1	14.5	12.5	12.8	11.6
2	11.6	12.9	12.3	11.1
3	12.7	12.6	11.6	11.0
4	10.3	11.9	11.4	10.3
5	9.7	10.9	10.4	10.7
6	11.5	11.3	11.2	10.1
8	10.4	10.3	10.6	11.6
10	9.8	11.2	9.8	11.2
24	11.5	10.9	10.0	10.7
	Phosphorus			
0	8.6	9.2	8.1	6.3
0.5	8.4	9.0	7.2	5.9
1	8.0	8.5	7.1	6.1
2	7.6	8.4	7.0	6.0
3	7.6	9.2	7.1	5.7
4	7.9	9.4	6.2	5.5
5	5.9	8.2	6.5	5.6
6	7.1	8.7	6.9	5.8
8	6.9	7.6	6.6	5.8
10	6.8	7.4	6.5	6.0
24	7.9	8.6	7.5	6.2

TABLE 23 (continued)

Hours	Thyroid-damaged		Control	
	121	251	253	271
	(mg/100 ml)			
	Magnesium			
0	2.20	2.14	2.86	2.34
0.5	2.30	2.43	2.54	2.26
1	2.22	2.27	2.01	1.91
2	2.19	2.18	2.37	1.91
3	2.04	2.28	2.28	2.08
4	1.93	2.11	2.51	2.11
5	1.90	2.16	2.34	2.16
6	2.02	2.18	2.33	2.07
8	1.82	2.12	1.98	1.80
10	1.98	1.99	2.18	2.10
24	1.95	2.02	1.98	2.45

[1]First 24 hours after dosing.

TABLE 24. Individual serum calcium, phosphorus, and magnesium concentration of calves used in Part 2 of Experiment 8[1]

Hour	Thyroid-damaged			Control		
	119	120	124	252	564	565
	(mg/100 ml)					
	Calcium					
0	10.2	10.4	10.4	10.4	10.3	10.2
0.5	14.2	13.5	13.0	13.4	13.4	12.8
1	12.9	11.7	12.1	10.8	11.8	11.0
2	12.4	10.7	10.7	9.0	9.7	10.5
3	11.6	10.7	11.0	10.4	10.9	11.2
4	10.8	9.9	10.3	9.4	9.5	9.9
5	10.4	10.9	10.0	9.4	11.3	10.7
6	10.3	10.9	10.8	9.7	9.9	10.8
8	10.6	10.3	10.1	10.6	10.8	10.3
10	11.0	10.7	10.3	10.9	10.0	9.9
12	10.4	10.5	10.7	11.0	10.0	10.5
24	9.5	11.1	10.0	10.4	10.6	9.5
	Phosphorus					
0	8.0	7.8	7.5	7.4	7.3	7.8
0.5	8.1	7.6	7.9	8.2	8.0	8.5
1	8.2	7.3	7.7	7.0	8.1	7.1
2	7.7	5.4	6.4	7.3	7.9	8.0
3	7.3	6.4	7.3	7.0	7.7	7.4
4	6.9	6.3	6.6	7.3	7.2	7.2
5	6.4	5.8	6.4	6.8	7.5	7.2
6	6.6	7.0	6.9	7.2	8.0	7.7
8	6.8	7.4	7.0	6.9	7.1	7.8
10	6.9	7.4	7.0	7.0	7.4	7.6
12	7.2	6.6	7.0	7.3	6.5	6.4
24	6.6	6.6	6.9	7.5	7.5	7.3

TABLE 24 (continued)

Hour	Thyroid-damaged			Control		
	119	120	124	252	564	565
	(mg/100 ml)					
	Magnesium					
0	2.63	3.05	2.60	2.35	2.78	2.25
0.5	2.58	2.25	2.55	3.00	2.70	3.03
1	2.60	2.53	2.33	2.90	2.43	2.70
2	2.18	2.33	2.70	2.18	2.30	2.75
3	2.35	2.50	2.40	2.58	2.70	2.70
4	2.35	3.10	2.73	2.20	2.50	2.95
5	2.15	2.65	2.73	2.65	2.85	2.90
6	2.55	2.78	2.60	2.30	2.90	2.68
8	2.48	2.28	2.90	3.10	2.93	2.50
10	2.80	2.65	2.60	2.65	2.70	3.05
12	2.40	2.45	3.05	2.58	2.83	2.80
24	2.90	2.95	3.00	2.78	3.15	2.50

[1]First 24 hours after dosing.

TABLE 25. Individual serum calcium, phosphorus, and magnesium concentration of control and thyroid-damaged cows at parturition

Cow	Treatment	Precalving			Calving			Postcalving		
		Ca	P	Mg	Ca	P	Mg	Ca	P	Mg
		(mg/100 ml)								
464	Control	9.3	5.6	2.64	8.6	3.7	2.85	5.0	5.7	2.85
475	"	9.9	5.6	2.17	7.9	7.4	2.45	8.4	5.2	2.41
466	"	9.7	7.8	2.58	7.9	8.8	2.91	9.2	7.7	2.12
406	"	9.5	10.3	1.86	7.7	5.9	2.28	10.0	7.8	1.94
475	"	9.5	4.5	2.80	8.7	4.8	3.25	10.2	4.0	2.82
469	"	9.0	3.6	2.50	7.2	4.1	2.75	8.7	2.6	2.35
465	Thyroid-damaged	10.8	6.1	2.18	10.4	5.7	3.09	10.4	4.6	2.64
474	"	10.6	4.6	2.17	10.3	4.6	2.72	10.9	6.0	2.58
467	"	9.6	5.7	2.48	9.6	3.1	3.13	8.5	7.7	2.66
405	"	10.8	8.1	2.48	8.3	3.9	4.20	9.3	5.4	2.33
465	"	10.6	4.8	2.90	10.3	6.4	3.34	10.2	4.1	2.61
189	"	10.0	9.8	1.94	8.1	7.3	2.02	10.3	10.0	2.44

TABLE 26. Individual serum calcium concentration of two calves infused with serum from normal and thyroid-damaged, parturient cows

Hours	Control cow serum		Thyroid-damaged cow serum	
	317	318	317	318
	(mg/100 ml)			
0	10.6	9.5	10.4	9.3
0.17	9.1	9.4	9.8	9.5
1	----	----	10.1	9.3
2	8.4	7.7	----	----
3	----	----	10.6	8.8
6	----	----	9.7	9.1
7	9.5	7.65	----	----
12	----	----	10.1	8.9
20	9.3	7.4	----	----
23	----	----	10.1	9.4
25	9.0	7.8	----	----

TABLE 27. Individual serum calcium, phosphorus, and magnesium concentration of calves used in Experiment 6[1]

Hours	Thyroid-damaged			Control		
	110	111	112	561	562	563
	(mg/100 ml)					
	Calcium					
0	12.0	10.7	10.4	11.0	10.9	10.3
0.5	10.5	9.7	11.0	11.2	9.7	9.6
1	10.6	10.3	10.4	10.4	10.3	11.0
2	11.3	10.2	11.3	11.4	10.3	9.9
4	12.1	11.7	11.1	10.7	11.6	12.0
6	11.6	9.7	10.8	11.5	10.2	10.5
8	11.6	10.1	9.6	10.3	9.8	11.0
10	11.4	10.9	10.5	10.7	10.9	10.3
12	10.8	9.9	9.8	10.1	10.4	10.1
24	9.8	9.9	10.6	10.3	9.7	10.4
48	11.5	9.9	10.9	10.4	9.8	9.7
72	9.6	10.3	11.2	10.3	9.3	10.4
	Phosphorus					
0	5.4	5.6	6.3	5.2	5.0	4.5
0.5	5.5	5.4	5.8	4.9	6.3	4.9
1	5.9	7.1	7.9	5.9	6.3	5.0
2	4.2	5.6	6.2	5.1	5.4	4.5
4	5.8	5.6	6.0	4.8	5.6	4.8
6	5.5	5.8	5.4	4.6	6.1	4.7
8	5.5	6.2	5.9	4.5	5.4	4.7
10	5.6	5.0	6.0	4.7	5.4	4.6
12	4.9	5.2	5.1	4.3	5.0	4.3
24	5.1	5.7	5.8	4.7	5.4	5.0
48	5.2	5.7	5.3	4.4	5.4	4.9
72	5.8	5.1	4.4	4.1	5.0	4.7

TABLE 27 (continued)

Hours	Thyroid-damaged			Control		
	110	111	112	561	562	563
	(mg/100 ml)					
	Magnesium					
0	3.28	3.18	3.50	2.80	3.58	2.48
0.5	2.65	3.20	3.25	3.30	2.83	2.25
1	2.93	3.43	3.18	2.85	3.15	2.25
2	2.35	3.03	2.68	2.70	3.25	2.30
4	3.38	3.43	3.30	3.08	3.03	3.00
6	3.18	2.28	3.10	3.38	2.88	2.88
8	3.18	2.79	3.03	2.95	2.93	2.45
10	2.98	3.60	2.93	2.75	2.75	2.53
12	3.15	2.95	2.63	2.88	3.30	2.43
24	2.55	3.03	2.98	2.80	3.05	2.15
48	2.53	2.88	2.65	2.18	2.85	2.00
72	2.38	2.73	2.80	2.63	2.80	2.23

[1]First 72 hours after dosing.

TABLE 28. Individual hourly serum ^{47}Ca and ^{45}Ca specific activity of calves used in Experiment 6[1]

Hours	Thyroid-damaged			Control		
	110	111	112	561	562	563
	(% dose/Ca g)					
			^{47}Ca			
0.5	17.60	16.77	23.01	14.48	22.10	22.29
1	13.81	9.24	16.96	9.90	13.31	15.75
2	6.49	5.87	11.98	6.38	8.88	10.80
4	4.74	4.78	6.71	3.80	4.38	5.74
6	3.44	3.47	5.10	2.83	3.62	5.23
8	2.77	2.36	2.98	2.06	3.90	2.46
10	2.07	1.72	2.96	2.09	3.00	2.54
12	1.37	1.22	1.91	1.66	1.78	2.72
24	1.09	0.70	1.42	0.90	0.92	1.41
48	0.39	0.31	0.65	0.38	0.43	0.55
72	0.38	0.31	0.40	0.34	0.32	0.41
			^{45}Ca			
0.5	0.71	0.88	0.73	2.41	3.78	2.48
1	1.61	1.27	1.50	2.86	3.14	1.56
2	1.10	1.11	0.61	2.24	3.51	2.67
4	2.49	1.23	1.46	3.08	4.87	3.12
6	3.29	1.98	2.03	3.37	6.61	4.87
8	2.35	2.38	2.10	2.56	4.13	3.75
10	1.65	3.00	1.26	2.67	3.64	3.61
12	2.24	3.91	1.92	4.73	6.72	4.67
24	2.93	4.78	3.64	5.08	6.22	5.84
48	2.05	1.07	2.65	3.47	3.93	4.73
72	2.43	0.74	2.47	3.23	3.52	2.80

[1]First 72 hours after dosing.

TABLE 29. Daily intake, excretion, and balance data of calves used in Experiment 6

Day	Thyroid-damaged 110	111	112	Control 561	562	563
	Total feed intake (g)					
1	3480	4000	3260	2460	2110	1530
2	3560	4000	3360	2580	2180	1960
3	3600	4000	4000	2380	2130	1860
4	3910	4000	3800	2620	3020	2740
5	3540	4000	3420	2540	2440	2060
	Total DM intake (g)					
1	3040	3496	2849	2148	1843	1336
2	3110	3496	2936	2253	1904	1712
3	3145	3496	3496	2078	1861	1624
4	3417	3496	3321	2288	2638	2393
5	3093	3496	2988	2218	2132	1799
	DM digestibility (%)					
1	70.82	67.01	58.42	72.52	68.57	71.13
2	67.83	66.01	61.84	72.62	72.10	66.60
3	64.93	60.06	68.65	79.52	74.85	77.76
4	66.82	65.85	74.48	75.53	73.98	73.45
5	68.07	73.72	68.48	69.81	66.26	78.32
	Calcium intake (g)					
1	19.56	22.76	18.48	13.38	11.70	8.34
2	20.05	22.76	19.05	14.01	12.13	10.77
3	20.30	22.76	22.76	12.99	11.86	10.21
4	22.21	22.76	21.53	14.26	16.72	15.00
5	19.97	22.76	19.15	13.94	13.72	11.44
	Phosphorus intake (g)					
1	11.58	13.14	10.75	8.45	7.12	5.27
2	11.82	13.14	11.08	8.88	7.33	6.66
3	11.94	13.14	13.14	8.16	7.16	6.33
4	12.87	13.14	12.54	9.00	10.20	9.36
5	11.76	13.14	11.40	8.66	8.18	6.94

TABLE 29 (continued)

Day	Thyroid-damaged 110	111	112	Control 561	562	563
	Magnesium intake (g)					
1	7.47	8.94	7.22	4.82	4.38	2.99
2	7.73	8.94	7.43	5.02	4.56	3.96
3	7.84	8.94	8.94	4.70	4.46	3.75
4	8.69	8.94	8.39	5.13	6.24	5.46
5	7.67	8.94	7.34	5.10	5.26	4.28
	Fecal calcium excretion (g)					
1	15.24	22.87	24.03	8.96	6.75	7.79
2	20.51	18.43	17.96	8.37	10.73	9.94
3	19.52	24.84	17.57	5.33	6.62	7.97
4	23.00	22.31	15.47	10.18	10.62	6.85
5	16.01	29.63	17.60	9.48	10.22	6.00
	Urinary calcium excretion (g)					
1	0.16	0.11	0.08	0.14	0.06	0.06
2	0.11	0.18	0.18	0.09	0.06	0.24
3	0.20	0.21	0.20	0.10	0.06	0.14
4	0.11	0.17	0.13	0.11	0.06	0.12
5	0.08	0.20	0.25	0.11	0.06	0.14
	Fecal phosphorus excretion (g)					
1	9.73	13.77	11.78	8.77	6.00	5.29
2	13.07	11.60	13.70	6.28	10.33	6.40
3	11.16	13.61	10.62	4.79	5.57	4.87
4	13.62	10.12	8.06	9.17	7.60	4.66
5	9.26	13.70	8.88	6.59	7.67	4.01
	Urinary phosphorus excretion (g)					
1	0.47	1.15	0.30	2.23	1.47	1.51
2	0.27	0.65	0.18	1.33	0.49	1.19
3	0.26	0.41	0.24	1.25	0.48	1.29
4	0.10	0.54	0.10	1.42	0.69	1.33
5	0.07	0.22	0.08	1.21	0.54	0.75

TABLE 29 (continued)

Day	Thyroid-damaged 110	111	112	Control 561	562	563
	Fecal magnesium excretion (g)					
1	4.86	7.18	7.82	3.82	2.90	2.33
2	5.49	9.59	6.34	3.39	4.76	3.08
3	6.03	7.11	6.20	2.30	2.61	2.42
4	6.70	6.67	5.17	4.07	3.94	2.07
5	5.19	8.78	6.16	4.30	4.23	2.30
	Urinary magnesium excretion (g)					
1	3.65	2.05	1.72	1.41	0.95	1.28
2	2.12	1.87	1.57	0.94	0.55	1.05
3	2.51	1.72	2.05	0.66	1.11	1.27
4	2.13	2.34	1.74	0.35	1.45	1.03
5	1.94	2.08	1.09	0.78	1.36	1.03
	Calcium balance (g)					
1	+4.16	-0.22	-563	+4.28	+5.07	-0.49
2	-0.57	+4.15	+0.91	+5.55	+1.34	+0.59
3	+0.58	-2.30	+4.99	+7.56	+5.18	+2.10
4	-0.90	+0.28	+5.93	+3.97	+6.04	+8.03
5	+3.88	-7.07	+1.34	+4.35	+3.44	+5.30
	Phosphorus balance (g)					
1	+1.38	-1.78	-7.33	-2.55	-0.35	-1.53
2	-1.52	+0.89	-2.80	+1.27	-3.49	-0.93
3	+0.52	-0.88	+2.28	+2.12	+1.11	+0.17
4	-0.89	+2.48	+4.38	-1.59	+1.91	+3.37
5	+2.43	-0.78	+2.44	+0.86	-0.03	+2.18
	Magnesium balance (g)					
1	-1.04	-0.29	-2.32	-0.41	+0.53	-0.62
2	+0.12	+2.48	-0.48	+0.69	-0.75	-0.17
3	-0.70	+0.11	+0.69	+1.74	+0.74	+0.06
4	-0.14	-0.07	+1.48	+0.71	+0.85	+2.36
5	+0.54	-1.92	+0.09	+0.02	-0.33	+0.95

TABLE 30. Average daily intake, excretion, and balance data per kg body weight of calves used in Experiment 6

Identity	Thyroid-damaged			Control		
	110	111	112	561	562	563
Total feed intake (g/kg)	282	268	257	251	262	213
Total Dm intake (g/kg)	246	234	225	219	229	186
Intake of						
Calcium (g/kg)	0.159	0.152	0.146	0.137	0.146	0.117
Phosphorus (g/kg)	0.150	0.152	0.139	0.098	0.122	0.087
Magnesium (g/kg)	0.061	0.060	0.057	0.049	0.055	0.043
Fecal calcium (g/kg)	0.134	0.145	0.127	0.079	0.096	0.079
Urinary calcium (mg/kg)	1.01	1.14	1.27	1.08	0.68	1.52
Fecal phosphorus (g/kg)	0.082	0.078	0.079	0.067	0.079	0.054
Urinary phosphorus (mg/kg)	1.79	4.15	1.27	14.86	8.22	13.87
Fecal magnesium (g/kg)	0.041	0.043	0.043	0.034	0.040	0.027
Urinary magnesium (mg/kg)	18.60	14.30	12.10	8.40	11.00	13.00
Balance of						
Calcium (mg/kg)	+23.06	+ 6.49	+22.34	+56.33	+48.65	+35.97
Phosphorus (mg/kg)	+ 9.78	+ 9.78	+ 5.95	+ 4.91	+ 3.69	+ 5.31
Magnesium (mg/kg)	+ 1.86	+ 2.48	+ 3.05	+ 7.28	+ 3.72	+ 4.88

TABLE 31. Individual radiocalcium balance data for calves used in Experiment 6

Identity	Thyroid-damaged			Control		
	110	111	112	561	562	563
			^{47}Ca			
Fecal excretion						
(% dose)	16.16	8.95	13.64	6.62	7.87	4.64
(% dose/kg BW)	0.130	0.060	0.100	0.070	0.080	0.050
Urinary excretion						
(% dose)	0.63	0.20	0.58	0.32	0.25	0.30
(% dose/kg BW)	0.005	0.001	0.004	0.003	0.003	0.003
			^{45}Ca			
Fecal excretion						
(% dose)	28.86	38.12	38.89	29.12	22.19	27.21
(% dose/kg BW)	0.220	0.260	0.290	0.290	0.250	0.300
Urinary excretion						
(% dose)	0.89	1.14	0.83	0.70	0.64	0.80
(% dose/kg BW)	0.007	0.008	0.006	0.007	0.007	0.008
			^{45}Ca			
Digestive tract recovery (% dose)	1.44	1.00	2.74	1.89	0.85	1.49

TABLE 32. Individual estimates of calcium metabolism parameters in the calves used in Experiment 6

Identity	Thyroid-damaged			Control		
	110	111	112	561	562	563
Fecal endogenous calcium (g)	1.83	1.54	1.43	1.61	1.18	0.87
Fecal endogenous calcium (mg/kg)	14.20	10.20	10.70	16.10	13.30	9.40
True absorption of radiocalcium (%)	84.91	67.96	70.76	75.91	84.46	79.47
% oral ^{45}Ca retained	84.02	66.82	69.93	75.12	83.82	78.67
% absorbed ^{45}Ca retained	99.00	98.32	98.83	99.08	99.24	98.99
True digestibility of dietary calcium (%)	36.19	-7.41	25.19	41.73	38.61	57.70
"Available calcium" pool (g)	43.64	54.65	35.46	39.22	38.46	22.94
"Available calcium" pool 1/2 time (hrs)	19.22	18.70	22.89	17.28	18.10	15.85
% dose in rib						
^{47}Ca	0.50	0.39	0.52	0.41	0.39	0.39
^{45}Ca	0.32	0.27	0.34	0.42	0.36	0.32
% dose in femur						
^{47}Ca	3.81	3.80	3.04	4.07	3.81	3.64
^{45}Ca	2.64	2.36	2.32	3.68	3.92	3.32

TABLE 33. Individual hourly serum ^{47}Ca and ^{45}Ca specific activity of calves used in Experiment 7[1]

Hours	Thyroid-damaged		Control	
	121	251	253	271
	(% dose/Ca g)			
	^{47}Ca			
0.5	11.48	16.09	13.99	14.71
1	9.13	14.63	9.59	9.86
2	7.35	10.55	8.06	7.07
3	6.03	9.12	6.34	5.93
4	6.06	8.98	5.42	5.12
5	5.72	8.49	5.26	4.34
6	4.76	7.18	4.33	3.76
8.0	3.97	6.35	3.45	2.62
10	3.60	5.36	3.28	2.35
24	2.23	3.57	2.15	2.62
48	1.48	2.17	0.89	0.84
72	1.23	1.33	0.73	0.66
	^{45}Ca			
0.5	4.29	6.71	5.09	5.98
1	4.29	6.59	4.14	4.63
2	3.33	4.08	3.54	3.93
3	2.88	4.79	3.23	3.52
4	3.23	4.40	2.50	3.18
5	2.69	4.05	2.62	2.83
6	2.55	3.86	2.66	3.33
8.5	2.31	3.67	1.89	1.83
10	1.92	3.41	2.33	2.39
24	1.03	2.46	1.51	0.91
48	0.49	0.97	0.76	0.56
72	0.40	0.55	0.68	0.06

[1]First 72 hours after dosing.

TABLE 34. Daily intake, excretion, and balance data of calves used in Experiment 7

Day	Thyroid-damaged		Control	
	121	251	253	271
	Total feed intake (g)			
1	5200	2240	4020	3960
2	4000	3040	4000	3780
3	4000	2870	4000	3640
4	5400	3300	4000	4430
5	4000	2100	4000	4000
	Total DM intake (g)			
1	4692	2017	3619	3564
2	3600	2740	3600	3400
3	3600	2577	3600	3277
4	4874	2964	3600	3992
5	3600	1884	3600	3600
	DM digestibility (%)			
1	81.91	73.08	78.61	74.85
2	70.60	81.04	67.43	73.26
3	63.28	78.98	65.67	63.89
4	74.83	81.92	68.87	80.17
5	65.21	74.36	67.63	70.89
	Calcium intake (g)			
1	33.17	14.00	25.06	24.65
2	24.92	19.15	24.92	23.42
3	24.92	17.50	24.92	22.46
4	34.48	20.14	24.92	27.86
5	24.92	12.06	24.92	24.92
	Phosphorus intake (g)			
1	16.19	7.24	13.05	12.89
2	13.00	9.67	13.00	12.41
3	13.00	9.70	13.00	12.05
4	16.72	11.14	13.00	14.14
5	13.00	7.24	13.00	13.00

TABLE 34 (continued)

Day	Thyroid-damaged 121	Thyroid-damaged 251	Control 253	Control 271
	Magnesium intake (g)			
1	11.82	4.60	8.12	7.94
2	8.06	6.53	8.06	7.37
3	8.06	5.09	8.06	6.93
4	12.44	5.87	8.06	9.41
5	8.06	3.45	8.06	8.06
	Fecal calcium excretion (g)			
1	15.65	10.08	15.36	19.98
2	20.34	7.95	27.56	30.59
3	23.18	13.86	22.17	19.31
4	27.52	10.53	22.04	16.30
5	25.75	10.67	31.13	29.57
	Urinary calcium excretion (g)			
1	0.34	0.29	0.21	0.44
2	0.19	0.35	0.18	0.45
3	0.12	0.43	0.26	0.25
4	0.22	0.16	0.20	0.15
5	0.25	0.23	0.10	0.13
	Fecal phosphorus excretion (g)			
1	7.69	5.60	6.71	7.63
2	7.20	4.43	8.81	9.01
3	9.89	6.79	10.00	8.61
4	12.80	6.17	9.54	7.45
5	11.37	6.27	9.18	14.22
	Urinary phosphorus excretion (g)			
1	0.23	0.22	0.16	0.33
2	0.17	0.26	0.62	0.30
3	0.11	0.84	0.10	0.15
4	0.10	0.10	0.12	0.12
5	0.14	0.11	0.14	0.09

TABLE 34 (continued)

Day	Thyroid-damaged 121	Thyroid-damaged 251	Control 253	Control 271
	Fecal magnesium excretion (g)			
1	4.56	3.40	6.33	7.18
2	6.66	2.87	10.51	7.94
3	6.86	4.44	9.03	6.06
4	7.47	3.28	6.70	4.75
5	7.03	2.96	8.76	8.22
	Urinary magnesium excretion (g)			
1	2.36	0.54	0.38	1.51
2	1.70	1.22	1.56	1.74
3	1.57	1.50	1.53	1.32
4	2.22	0.63	1.09	1.12
5	2.75	0.97	1.17	0.68
	Calcium balance (g)			
1	+17.13	+ 3.63	+ 9.49	+ 4.23
2	+ 4.39	+10.85	+ 2.82	- 7.62
3	+ 1.62	+ 3.21	+ 2.49	+ 2.90
4	+ 6.72	+ 9.49	+ 2.68	+11.41
5	- 1.08	+ 1.76	- 6.31	- 4.78
	Phosphorus balance (g)			
1	+ 8.27	+ 1.42	+ 6.18	+ 4.93
2	+ 5.63	+ 4.98	+ 3.57	+ 3.10
3	+ 3.00	+ 2.07	+ 2.90	+ 3.29
4	+ 3.82	+ 4.87	+ 3.34	+ 6.57
5	+ 1.49	+ 0.86	+ 3.68	- 1.31
	Magnesium balance (g)			
1	+ 3.28	- 0.31	- 0.39	- 2.55
2	- 2.10	+ 1.23	- 5.81	- 4.11
3	- 2.17	- 2.43	- 4.30	- 2.25
4	+ 0.85	+ 0.16	- 1.53	+ 1.74
5	- 3.52	- 1.74	- 3.67	- 2.64

TABLE 35. Individual radiocalcium balance data for calves used in Experiment 7

Identity	Thyroid-damaged		Control	
	121	251	253	271
		^{47}Ca		
Fecal excretion (% dose)	18.12	17.01	17.63	11.38
Urinary excretion (% dose)	2.60	3.23	2.92	2.48
		^{45}Ca		
Fecal excretion (% dose)	52.19	44.12	60.70	60.34
Urinary excretion (% dose)	0.63	1.30	0.82	0.85
Digestive tract recovery (% dose)	7.38	11.25	6.09	6.03

TABLE 36. Individual estimates of calcium metabolism parameters in calves used in Experiment 7

Identity	Thyroid-damaged		Control	
	121	251	253	271
Fecal endogenous calcium (g)	1.93	1.20	2.32	0.66
True absorption of radiocalcium (%)	58.39	67.33	47.71	44.75
% ^{45}Ca retained	57.76	66.03	46.89	43.92
% absorbed ^{45}Ca retained	98.92	98.07	98.28	98.15
True digestibility of dietary calcium (%)	14.50	38.20	2.03	13.47
"Available calcium" pool (g)	26.81	15.82	25.77	29.07
"Available calcium" pool 1/2 time (hrs)	39.15	41.93	26.76	25.55
% dose in rib				
^{47}Ca	0.63	1.11	0.88	0.16
^{45}Ca	0.19	0.24	0.23	0.18
% dose in femur				
^{47}Ca	3.43	6.00	4.54	1.03
^{45}Ca	1.79	1.42	1.40	1.00

TABLE 37. Individual hourly serum ^{47}Ca and ^{45}Ca specific activity of calves used in Parts 2 and 3 of Experiment 8[1]

Hours	Thyroid-damaged			Control		
	119	120	124	252	564	565
	(% dose/Ca g)					
	^{47}Ca					
0.5	9.09	9.16	11.12	12.59	11.19	9.39
1	6.92	8.04	9.88	11.14	9.20	8.77
2	5.71	5.76	7.24	9.41	7.19	7.50
3	4.58	4.40	5.50	6.96	5.43	5.03
4	4.36	3.97	5.42	6.38	4.79	5.10
5	4.04	3.72	4.35	5.16	3.78	3.93
6	3.76	2.71	3.76	4.25	4.60	3.40
8	2.72	2.56	3.24	2.94	2.71	3.14
10	2.40	1.86	2.70	2.32	2.50	2.48
12	2.14	1.74	2.33	2.00	1.94	2.36
24	1.38	0.99	1.64	1.11	1.07	1.54
48	0.57	0.67	0.96	0.87	0.95	0.92
72	0.47	0.49	0.85	0.72	0.90	1.00
	^{45}Ca					
4	1.70	1.35	2.95	3.22	3.45	2.14
10.5	3.02	2.07	3.16	3.44	4.74	3.90
24	6.44	5.68	4.76	4.17	8.35	8.65
48	2.70	4.51	1.08	4.01	3.30	5.97
72	1.78	2.68	1.94	0.99	2.44	2.81

[1]First 72 hours after dosing.

TABLE 38. Daily intake, excretion, and balance data of calves in Part 2 of Experiment 8

Day	Thyroid-damaged			Control		
	119	120	124	252	564	565
	Total feed intake (g)					
1	4360	4100	4340	3360	4160	4220
2	4300	4200	4360	3980	4260	4160
3	4400	3980	4400	3980	4240	4340
4	3800	4220	4400	4160	4260	4400
5	4400	4400	4400	4160	4240	4280
	Total DM intake (g)					
1	3967	3731	3949	3057	3785	3840
2	3913	3822	3967	3621	3876	3785
3	4004	3621	4004	3621	3858	3949
4	3458	3840	4004	3785	3876	4004
5	4004	4004	4004	3785	3858	3894
	DM digestibility (%)					
1	67.31	66.79	67.14	65.55	61.71	68.76
2	65.30	66.03	61.51	66.81	61.09	58.79
3	72.72	69.88	65.43	68.09	60.94	65.76
4	69.80	65.49	66.92	65.55	63.20	61.61
5	59.69	60.87	63.39	65.25	62.07	61.18
	Calcium intake (g)					
1	29.03	27.07	28.88	21.50	27.53	27.98
2	28.58	27.83	29.03	26.17	28.28	27.52
3	29.33	26.17	29.33	26.17	28.13	28.88
4	24.81	27.98	29.33	27.53	28.28	29.33
5	29.33	29.33	29.33	27.12	28.13	28.43
	Phosphorus intake (g)					
1	13.91	13.22	13.86	11.27	13.38	13.54
2	13.75	13.49	13.91	12.91	13.65	13.38
3	14.02	12.91	14.02	12.91	13.59	13.86
4	12.43	13.54	14.02	13.38	13.65	14.02
5	14.02	14.02	14.02	13.38	13.59	13.70

TABLE 38 (continued)

Day	Thyroid-damaged 119	120	124	Control 252	564	565
	Magnesium intake (g)					
1	7.82	7.16	7.77	5.27	7.31	7.46
2	7.67	7.41	7.82	6.85	7.56	7.31
3	7.92	6.85	7.92	6.85	7.51	7.77
4	6.39	7.46	7.92	7.31	7.56	7.92
5	7.92	7.92	7.92	7.31	7.51	7.61
	Fecal calcium excretion (g)					
1	19.73	13.04	20.07	17.07	23.83	13.31
2	20.28	18.42	20.25	19.05	27.42	19.60
3	13.92	19.47	17.66	17.17	13.42	18.59
4	8.56	23.59	17.37	22.68	16.34	16.54
5	27.65	34.61	23.98	23.73	29.70	27.96
	Urinary calcium excretion (g)					
1	0.08	0.10	0.18	0.10	0.11	0.13
2	0.28	0.09	0.17	0.07	0.06	0.09
3	0.26	0.07	0.07	0.06	0.04	0.13
4	0.16	0.06	0.07	0.07	0.06	0.09
5	0.16	0.08	0.09	0.12	0.12	0.12
	Fecal phosphorus excretion (g)					
1	12.05	13.66	12.73	10.81	14.75	10.24
2	9.97	12.35	16.65	11.53	17.49	11.08
3	7.91	10.98	15.14	10.68	10.47	11.57
4	9.22	13.18	15.67	16.32	14.50	14.74
5	18.84	17.14	11.59	11.54	17.04	15.05
	Urinary phosphorus excretion (g)					
1	0.34	0.78	0.85	0.88	0.27	0.96
2	0.51	0.55	0.71	0.34	0.40	0.57
3	0.57	0.43	0.83	0.39	0.40	0.36
4	0.63	0.36	0.80	0.24	0.35	0.24
5	0.50	0.62	0.75	0.35	0.41	0.34

TABLE 38 (continued)

Day	Thyroid-damaged 119	120	124	Control 252	564	565
	Fecal magnesium excretion (g)					
1	6.39	4.53	6.40	5.23	7.88	5.19
2	6.28	5.71	5.85	6.82	10.09	7.54
3	4.60	6.85	6.53	4.71	6.38	7.67
4	4.07	8.01	5.49	10.96	6.48	6.62
5	10.54	8.28	8.89	9.26	12.52	7.49
	Urinary magnesium excretion (g)					
1	1.27	2.75	1.97	2.11	1.69	2.79
2	2.64	2.55	1.17	1.80	1.91	2.11
3	2.91	2.84	1.59	1.69	1.51	2.64
4	3.26	2.73	1.48	1.77	1.80	2.53
5	2.42	2.89	1.75	2.54	1.89	2.87
	Calcium balance (g)					
1	+ 9.22	+13.93	+ 8.36	+ 4.33	+ 3.59	+14.54
2	+ 8.02	+ 9.32	+ 8.61	+ 7.05	+ 0.80	+ 7.83
3	+15.15	+ 6.63	+11.60	+13.94	+14.67	+10.16
4	+16.09	+ 4.33	+11.89	+ 4.78	+12.38	+12.70
5	+ 1.52	- 5.36	+ 5.26	+ 3.17	- 1.69	+ 0.35
	Phosphorus balance (g)					
1	+ 1.52	- 1.22	+ 0.28	- 0.42	- 1.64	+ 2.34
2	+ 3.27	+ 0.59	- 3.45	+ 1.13	- 4.24	+ 1.73
3	+ 5.54	+ 1.51	- 1.95	+ 1.84	+ 2.72	+ 1.93
4	+ 2.58	0.00	- 2.45	- 3.18	- 1.20	- 0.96
5	- 5.32	- 3.74	+ 1.68	+ 1.49	- 3.86	- 1.69
	Magnesium balance (g)					
1	+ 1.60	- 0.12	- 0.60	- 2.07	- 2.26	- 0.52
2	- 1.25	- 0.85	+ 0.80	- 1.77	- 4.44	- 2.34
3	+ 0.41	- 2.84	- 0.20	+ 0.45	- 0.38	- 2.54
4	- 0.94	- 3.28	+ 0.95	- 5.42	- 0.72	- 1.23
5	- 5.04	- 3.25	- 2.72	- 4.49	- 6.90	- 2.75

TABLE 39. Daily intake, excretion, and balance data of calves in Part 3 of Experiment 8

Day	Thyroid-damaged			Control		
	119	120	124	252	564	565
	Total feed intake (g)					
1	4400	4400	4400	4400	4400	4400
2	4400	4400	4400	4400	4400	4400
3	4400	4400	4400	4400	4400	4400
4	4400	4340	4400	4400	4400	4400
5	4400	4400	4400	4400	4250	4400
	Total DM intake (g)					
1	4002	4002	4002	4002	4002	4002
2	4002	4002	4002	4002	4002	4002
3	4002	4002	4002	4002	4002	4002
4	4002	3947	4002	4002	4002	4002
5	4002	4002	4002	4002	3866	4002
	DM digestibility (%)					
1	64.62	60.22	64.88	56.11	64.39	58.49
2	65.85	68.73	70.57	68.79	68.23	63.30
3	65.20	67.20	71.72	64.79	65.06	64.45
4	61.61	67.58	64.97	64.11	71.07	61.05
5	63.83	61.35	67.94	71.71	67.77	63.16
	Calcium intake (g)					
1	27.65	27.65	27.65	27.65	27.65	27.65
2	27.65	27.65	27.65	27.65	27.65	27.65
3	27.65	27.65	27.65	27.65	27.65	27.65
4	27.65	27.24	27.65	27.65	27.65	27.65
5	27.65	27.65	27.65	27.65	26.64	27.65
	Phosphorus intake (g)					
1	14.06	14.06	14.06	14.06	14.06	14.06
2	14.06	14.06	14.06	14.06	14.06	14.06
3	14.06	14.06	14.06	14.06	14.06	14.06
4	14.06	13.90	14.06	14.06	14.06	14.06
5	14.06	14.06	14.06	14.06	13.67	14.06

TABLE 39 (continued)

Day	Thyroid-damaged 119	Thyroid-damaged 120	Thyroid-damaged 124	Control 252	Control 565	Control 565
	Magnesium intake (g)					
1	9.31	9.31	9.31	9.31	9.31	9.31
2	9.31	9.31	9.31	9.31	9.31	9.31
3	9.31	9.31	9.31	9.31	9.31	9.31
4	9.31	9.12	9.31	9.31	9.31	9.31
5	9.31	9.31	9.31	9.31	8.84	9.31
	Fecal calcium excretion (g)					
1	18.38	21.16	22.84	21.97	15.82	18.09
2	16.24	14.94	20.33	11.45	15.03	13.65
3	24.39	18.06	16.47	20.65	19.17	17.09
4	20.74	20.08	18.00	21.74	12.53	20.17
5	20.76	21.28	20.95	15.46	19.02	17.07
	Urinary calcium excretion (g)					
1	0.24	0.10	0.09	0.09	0.12	0.25
2	0.07	0.19	0.13	0.05	0.07	0.06
3	0.19	0.15	0.15	0.44	0.22	0.08
4	0.19	0.20	0.26	0.15	0.16	0.16
5	0.08	0.13	0.13	0.10	0.40	0.09
	Fecal phosphorus excretion (g)					
1	8.48	9.99	7.47	10.47	7.65	8.36
2	7.58	6.91	6.55	6.61	7.22	5.00
3	8.00	6.44	4.82	8.79	9.82	9.11
4	9.29	7.63	6.66	11.30	5.85	6.70
5	8.07	7.04	7.32	5.01	7.77	6.21
	Urinary phosphorus excretion (g)					
1	0.08	0.07	0.08	0.04	0.03	0.03
2	0.05	0.07	0.25	0.06	0.04	0.04
3	0.21	0.12	0.13	0.14	0.08	0.05
4	0.11	0.12	0.09	0.06	0.07	0.07
5	0.09	0.09	0.09	0.06	0.13	0.07

TABLE 39 (continued)

Day	Thyroid-damaged 119	Thyroid-damaged 120	Thyroid-damaged 124	Control 252	Control 564	Control 565
	Fecal magnesium excretion (g)					
1	6.77	7.72	6.81	7.21	6.40	7.00
2	5.59	4.89	7.17	3.92	5.95	5.07
3	8.75	6.79	5.73	7.41	7.28	6.78
4	6.12	7.24	5.75	7.70	5.07	7.50
5	5.51	6.13	5.83	5.06	7.02	5.43
	Urinary magnesium excretion (g)					
1	1.84	1.60	1.46	1.93	1.74	1.51
2	1.14	1.72	0.94	1.03	0.96	1.48
3	4.26	2.86	1.21	4.78	2.31	2.23
4	2.74	3.32	1.28	2.75	2.24	2.25
5	2.69	3.07	2.04	2.90	2.40	2.16
	Calcium balance (g)					
1	+ 9.03	+ 5.89	+ 4.72	+ 5.59	+11.71	+ 9.31
2	+11.34	+12.52	+ 7.19	+16.15	+12.55	+13.93
3	+ 3.07	+ 9.44	+11.03	+ 6.59	+ 8.26	+10.48
4	+ 6.72	+ 6.96	+ 9.39	+ 5.76	+14.96	+ 7.32
5	+ 7.31	+ 6.24	+ 6.57	+12.09	+ 7.22	+10.49
	Phosphorus balance (g)					
1	+ 5.50	+ 4.00	+ 6.49	+ 3.55	+ 6.38	+ 5.67
2	+ 6.43	+ 7.08	+ 7.26	+ 7.39	+ 6.80	+ 9.02
3	+ 5.85	+ 7.50	+ 9.11	+ 5.13	+ 4.16	+ 4.90
4	+ 4.66	+ 6.15	+ 7.31	+ 2.07	+ 8.14	+ 7.29
5	+ 5.90	+ 6.93	+ 6.65	+ 9.00	+ 6.16	+ 7.78
	Magnesium balance (g)					
1	+ 0.70	+ 0.01	+ 1.04	+ 0.17	+ 1.17	+ 0.80
2	+ 2.58	+ 2.70	+ 1.20	+ 4.36	+ 2.40	+ 2.76
3	- 3.70	+ 0.34	+ 2.37	- 2.88	- 0.28	+ 0.30
4	+ 0.45	- 1.44	+ 2.28	- 1.14	- 1.53	- 0.44
5	+ 1.11	+ 0.11	+ 1.44	+ 1.35	- 0.11	+ 1.72

TABLE 40. Individual radiocalcium balance data for calves in Parts 2 and 3 of Experiment 8

Identity	Thyroid-damaged			Control		
	119	120	124	252	564	565
			^{47}Ca			
Fecal excretion (% dose)	8.62	7.41	11.07	10.35	10.35	7.54
Urinary excretion (% dose)	0.72	0.56	0.87	0.84	0.89	0.66
			^{45}Ca			
Fecal excretion (% dose)	33.55	42.19	38.29	32.41	38.12	35.89
Urinary excretion (% dose)	0.97	1.40	1.79	1.50	2.33	1.30
Digestive tract recovery (% dose)	3.99	5.13	5.31	12.37	3.29	2.09

TABLE 41. Individual estimates of calcium metabolism parameters in calves used in Experiment 8

Identity	Thyroid-damaged			Control		
	119	120	124	252	564	565
Endogenous fecal calcium (g)	0.89	0.69	0.80	1.38	1.16	0.69
True absorption of radiocalcium (%)	72.70	62.43	69.42	75.41	69.06	69.31
% oral ^{45}Ca retained	71.73	60.94	67.63	73.91	66.73	68.01
% absorbed ^{45}Ca retained	98.67	97.61	97.42	98.01	96.62	98.12
True digestibility of dietary calcium (%)	38.28	13.82	34.33	28.99	34.10	30.04
"Available calcium" pool (g)	29.93	47.39	32.79	44.25	48.54	32.69
"Available calcium" pool 1/2 time (hrs)	18.74	27.80	28.91	32.58	39.00	27.12

TABLE 42. Daily milk production, radiocalcium content, and milk: plasma ratios of cows used in Experiment 9

Day	Milking	Without TSH		With TSH	
		Thyroid-damaged	Control	Thyroid-damaged	Control
		Milk yield (kg/day)			
1		4.01	8.17	4.15	9.89
2		4.59	8.42	4.32	11.25
3		4.28	8.64	4.90	11.69
4		5.12	10.23	3.35	6.75
5		4.67	9.31	4.63	10.89
		% dose in milk/day			
1		11.62	50.71	11.60	29.39
2		5.65	13.23	5.49	9.51
3		2.27	5.90	3.04	4.00
4		1.72	3.58	1.39	1.55
5		1.02	2.17	1.20	1.38
		Milk:plasma ratio of radiocalcium			
1	PM	6.97	8.20	7.51	14.55
	AM	19.70	49.49	12.95	20.84
2	PM	14.65	27.47	18.52	8.61
	AM	15.59	26.73	24.95	9.16
3	PM	14.46	17.68	9.37	11.21
	AM	15.76	31.13	9.28	9.71
4	PM	15.11	26.75	8.96	9.21
	AM	11.24	27.44	7.51	8.74
5	PM	-----	-----	7.34	8.82
	AM	-----	-----	7.12	11.60

TABLE 43. Individual milk yield, milk radiocalcium, milk:plasma ratios, milk calcium, and endogenous calcium for the cows used in Experiment 10

Day	Milking	With thyroxine therapy			Without thyroxine therapy		
		Thyroid-damaged	Control	Control	Thyroid-damaged	Control	Control
		Milk yield (kg/day)					
1		15.12	6.22	10.31	1.36	8.31	6.81
2		14.12	7.22	9.49	1.45	8.85	8.31
3		14.21	8.17	11.08	2.00	9.40	8.81
4		15.53	9.85	11.35	0.77	9.04	7.99
5		14.98	9.67	11.08	0.95	9.17	8.26
6		13.76	10.67	11.80	----	----	----
7		14.03	10.81	11.53	----	----	----
		Milk radiocalcium (% dose/day)					
1		29.54	11.14	19.98	2.34	10.77	10.04
2		8.62	6.73	1.58	2.25	6.69	4.26
3		5.80	3.08	3.64	2.64	2.56	2.12
4		3.34	1.56	3.38	0.46	3.38	1.23
5		1.45	1.54	0.87	0.95	0.86	0.76
6		0.70	1.29	0.83	----	----	----
7		0.78	0.56	0.81	----	----	----
		Milk:plasma ratio of radiocalcium					
1	PM	9.17	5.63	9.04	0.76	3.11	4.96
	AM	19.91	15.63	17.63	9.52	15.31	13.04
2	PM	20.82	7.67	13.65	9.95	14.14	9.95
	AM	14.30	24.49	21.10	14.14	19.62	12.77
3	PM	12.48	8.72	18.00	16.60	11.20	8.51
	AM	29.65	15.46	11.71	19.68	12.40	11.17
4	PM	11.00	21.46	19.50	14.22	10.18	10.63
	AM	22.73	7.24	21.85	19.10	16.50	15.89
5	PM	9.28	14.40	9.81	22.74	20.89	11.81
	AM	11.00	9.57	5.75	47.22	7.00	11.40
6	PM	5.00	11.57	7.80	----	----	----
	AM	6.33	8.83	7.67	----	----	----
7	PM	5.10	3.28	6.46	----	----	----
	AM	7.50	5.10	7.20	----	----	----

TABLE 43 (continued)

Day	Milking	With thyroxine therapy: Thyroid-damaged	With thyroxine therapy: Control	Control	Without thyroxine therapy: Thyroid-damaged	Without thyroxine therapy: Control	Control
		Milk calcium (g/day)					
1		18.24	7.73	11.47	2.54	13.14	10.46
2		16.82	9.06	12.39	1.69	7.98	8.47
3		16.08	9.32	12.91	2.91	13.00	7.35
4		18.42	12.06	12.83	0.68	11.24	11.33
5		16.22	11.26	13.07	1.59	8.24	8.40
6		14.51	11.27	14.47	----	----	----
7		15.54	12.18	13.15	----	----	----
		Endogenous calcium (g/day)					
1		----	----	----	----	----	----
2		----	----	----	1.84	4.76	4.47
3		----	----	----	1.46	4.70	5.12
4		14.27	7.64	7.92	4.00	8.30	10.60
5		5.00	10.00	5.00	1.30	5.29	15.40
6		3.38	9.40	7.75	----	----	----
7		10.29	9.38	5.38	----	----	----

TABLE 44. Percentage of radiocalcium dose transferred to the fetus by thyroid-damaged and control cows

Cow	Treatment	Days after dosing	% Dose transferred
292	Thyroid-damaged	17	45.57
465	" "	7	34.85
467	" "	18	36.27
157	Control	8	26.67
466	"	7	39.22
930	"	15	38.88

VITA

William Francis Byrne was born the second son of James Joseph and Mary Elsie Byrne September 1, 1940 at Nashville, Tennessee. He received his elementary education in the Nashville Parochial school system and was graduated from Father Ryan High School, Nashville, Tennessee in 1958. He entered the University of Tennessee in September of 1958 but withdrew for health reasons. For the next three years he worked in the Nashville area. He entered the College of Agriculture at the University of Tennessee in September of 1961, majoring in Dairying. In September, 1962 he transferred to Middle Tennessee State University, Murfreesboro, Tennessee where he majored in Agriculture until January, 1963. In March of 1963 he returned to the University of Tennessee College of Agriculture to continue his studies in Dairying. He received the Bachelor of Science degree with honors in March of 1965.

He entered the Graduate School at the University of Tennessee in March, 1965 and served as an Assistant-in-Dairying from that time until September, 1965 at which time he accepted an NDEA Fellowship in Animal Science. He resigned that fellowship in September, 1966. In January, 1967 he was reappointed an Assistant-in-Dairying in which capacity he served until November of 1968. At that time he was employed by the University of Tennessee-Atomic Energy Commission Agricultural Research Laboratory at Oak Ridge as a Senior Laboratory Technician. He received the Master of Science degree in March of 1967. He is a member of Phi Kappa Phi and Gamma Sigma Delta honorary societies and the American Dairy Science Association.