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THE EFFECTS OF INSULIN, GLUCOSE AND CATECHOLAMINES ON SOME BLOOD MINERALS IN SHEEP

By

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PERSSON, J. & J. LUTHMAN: *The effects of insulin, glucose and catecholamines on some blood minerals in sheep.* Acta vet. scand. 1974, *15*, 519—532. — Intravenous injection of insulin, 0.5 i.u./kg, was followed by a decrease in plasma magnesium. It is earlier known that insulin sometimes lowers the blood magnesium level, and the mechanism behind this effect is said to be an increased tissue uptake of magnesium. Glucose infusion did not change plasma magnesium, whereas norepinephrine and epinephrine caused a slight reduction. Insulin at the dose of 1 i.u./kg reduced plasma calcium in intact sheep. In thyroidectomized sheep the same dose caused a rise in plasma calcium. It is suggested that insulin caused hypercalcaemia in the thyroidectomized sheep by increasing the rate of bone resorption, and that the decrease in plasma calcium observed in the intact sheep was due to release of calcitonin to such an extent that the bone resorbing effect of insulin was blocked. Insulin also lowered plasma inorganic phosphorus in the thyroidectomized sheep.

insulin; glucose; catecholamines; calcium; magnesium; inorganic phosphorus.

In spite of a vast amount of research work, the metabolism and regulation of magnesium is still poorly understood. In a review, *Walser* (1967) stated that there does not seem to be any endocrine mechanism whose primary function is to regulate plasma magnesium.

Much attention has been paid to clarify the relationship between parathyroid hormone (PTH) and magnesium. The effects of PTH on magnesium is supposed to be qualitatively the same as that on calcium, but less pronounced (*Gill et al.* 1967, *Heaton* 1965). A feed back mechanism has been suggested since *Care et al.* (1966) and *Buckle et al.* (1968) showed that perfusion of

the parathyroids with blood containing magnesium above the normal level produced a decrease of PTH concentration in the systemic circulation.

In man, hyperthyroidism is often associated with negative magnesium balance (*Wacker & Parisi* 1968), and *Meyer & Schmidt* (1958) found that thyroxine caused a transient hypomagnesaemia in calves.

Negative magnesium balance is also found in hyperaldosteronism, and administration of aldosterone increases the renal excretion of magnesium (*Hanna & MacIntyre* 1960) and sometimes reduces the plasma magnesium level (*Scott & Dobson* 1965).

Insulin and glucose administration tends to lower plasma magnesium (*Whang et al.* 1966) as does glucagon (*Conte et al.* 1972). *Aikawa* (1960) found increased tissue magnesium content in rabbits after treatment with insulin and glucose. An intimate relationship thus seems to exist between magnesium and carbohydrate metabolism. Since this relationship has been poorly studied, the primary aim of the present investigation was to study the effects of some agents, known to affect carbohydrate metabolism, on the plasma magnesium level in sheep. During the performance of the experiments, *Puche et al.* (1973) reported that insulin induced bone resorption in rats. It was therefore considered of value to investigate if insulin affected calcium metabolism also in sheep.

MATERIAL AND METHODS

The animal material consisted of 50 sheep of both sexes, all female animals being non-pregnant. All animals were of the Swedish landrace. They were kept indoors and fed hay and grain twice a day. The animals were non-fasted when used in the experiments.

The effect of insulin on plasma magnesium was studied in a preliminary experiment. Insulin (Insulin Novo Actrapid, Novo, Malmö, Sweden) at a dose of 0.5 i.u./kg was injected intravenously via the jugular vein to 6 young sheep (6—9 months old). Blood was drawn in heparinized tubes (Heparinrör, Vitrum, Stockholm, Sweden). Control animals were given saline.

The effects of glucose, norepinephrine and epinephrine were studied in young sheep (6—9 months old). Glucose, at a dose of

0.3 g/kg, was infused intravenously at a constant rate during 60 min. by means of a peristaltic pump. Norepinephrine (Norexadrin conc., Astra, Södertälje, Sweden) and epinephrine (Adrenalin, ACO, Stockholm, Sweden), both at a dose of 1 μg/kg, were infused in the same manner. Control animals received only saline. Whole blood was analysed for glucose and plasma for magnesium.

The effects of insulin on calcium metabolism were investigated in 2 groups of animals, each consisting of 6 adult ewes. The first group received an intravenous injection of insulin at a dose of 1 i.u./kg. The animals in the second group were all thyroidectomized. Thyroidectomy was performed as described by *Luthman et al.* (1972). About 24 hrs. after surgery insulin was given as above. A group of intact ewes served as controls and received only saline. Whole blood was analysed for glucose and plasma for calcium, magnesium, inorganic phosphorus and non-esterified fatty acids (NEFA).

In order to avoid stress effects, plastic cannulas (Braunüle 2 L, Braun, Melsungen, Germany) were inserted into the jugular vein of all animals several hours before start of the experiments.

The pretreatment levels given in text, figures and tables are the mean of 2 determinations, at —30 min. and immediately before start of the experiment.

Blood glucose was analysed according to the glucose oxidase method (reagents from AB Kabi, Stockholm, Sweden). The method of *Skerry* (1965) was used for the determination of plasma calcium. Plasma NEFA was determined according to *Dole* (1956). Commercial reagent kits were used for the determination of plasma magnesium (Merckotest Magnesium, E. Merck, Darmstadt, Germany) and plasma inorganic phosphorus (Sigma Kit 670, Sigma Chemical Company, St. Louis, USA).

Conventional statistical methods were used (Student's t-test).

RESULTS

As seen in Fig. 1, insulin caused a linear decrease in plasma magnesium during 90 min.

The changes in blood glucose and plasma magnesium after intravenous infusion of glucose, norepinephrine and epinephrine in young sheep are given in Table 1. No significant changes in plasma magnesium were obtained after the infusion of glucose,

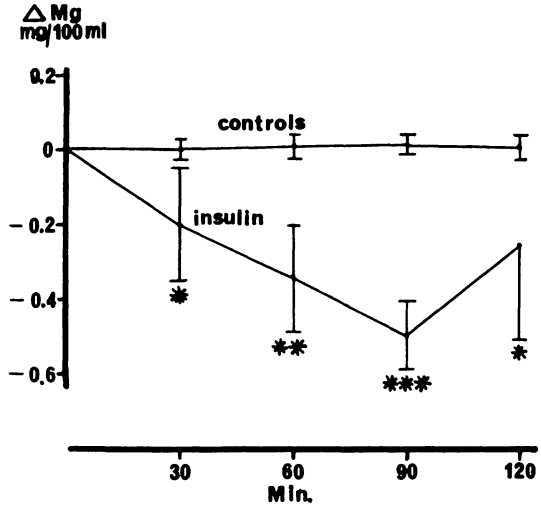

Figure 1. Changes in plasma magnesium in young sheep after intravenous injection of 0.5 i.u./kg of insulin. Pretreatment level was 2.45±0.20 mg/100 ml in the control group and 2.28±0.10 mg/100 ml in the insulin group.

* $0.05 > P > 0.01$
** $0.01 > P > 0.001$
*** $P < 0.001$

while norepinephrine caused an almost significant reduction ($0.05 > P > 0.01$). Epinephrine caused a similar reduction, but only 4 animals were used and no statistical calculations were made.

Fig. 2 shows the changes in blood glucose and plasma NEFA in intact and thyroidectomized adult ewes after intravenous injection of insulin, 1 i.u./kg. A pronounced hypoglycaemia was obtained in both groups. The decrease in blood glucose was greater in thyroidectomized than in intact animals, the difference in response was almost significant ($0.05 > P > 0.01$).

In both groups there was a small, but statistically significant, initial fall in plasma NEFA followed by a rebound elevation, which was significant in both groups. The rebound in NEFA was most pronounced in the intact animals, the difference between the groups was highly significant ($P < 0.001$) 30 min. and 3 hrs. after the injection.

Insulin caused significant hypocalcaemia in intact animals, whereas in thyroidectomized animals a significant increase in

Table 1. Changes in the plasma levels of glucose and magnesium during and after 60 min. intravenous infusion of glucose (0.3 g/kg), epinephrine (1 μg/kg/min.) and norepinephrine (1 μg/kg/min.). Mean±s.

	Pretreatment level	Minutes					
		30	60	90	120	150	180
				Δ Glucose mg/100 ml			
Controls (n=5)	46±3	+2±2	+3±4	+2±3	+2±2	+3±3	+2±1
Glucose (n=6)	51±3	+55±27	+62±11	+12±12	—1±6	—2±7	—1±6
Norepinephrine (n=5)	47±6	+69±27	+88±23	+76±19	+63±19	+50±18	+33±17
Epinephrine (n=4)	53±6	+128±31	+152±11	+148±16	+142±5	+132±25	+99±18
				Δ Mg mg/100 ml			
Controls (n=5)	2.36±0.26	0.00±0.12	—0.06±0.11	0.00±0.16	+0.06±0.11	+0.02±0.15	—0.02±0.16
Glucose (n=6)	2.65±0.24	—0.06±0.08	—0.03±0.10	+0.05±0.10	+0.03±0.10	+0.10±0.13	+0.15±0.10
Norepinephrine (n=5)	2.50±0.07	—0.06±0.09	—0.08±0.13	—0.22±0.04*	—0.15±0.13*	—0.16±0.05*	—0.12±0.11
Epinephrine (n=4)	2.25±0.24	—0.18±0.05	—0.25±0.10	—0.23±0.10	—0.18±0.10	—0.15±0.17	—0.08±0.15

* $0.05 > P > 0.01$

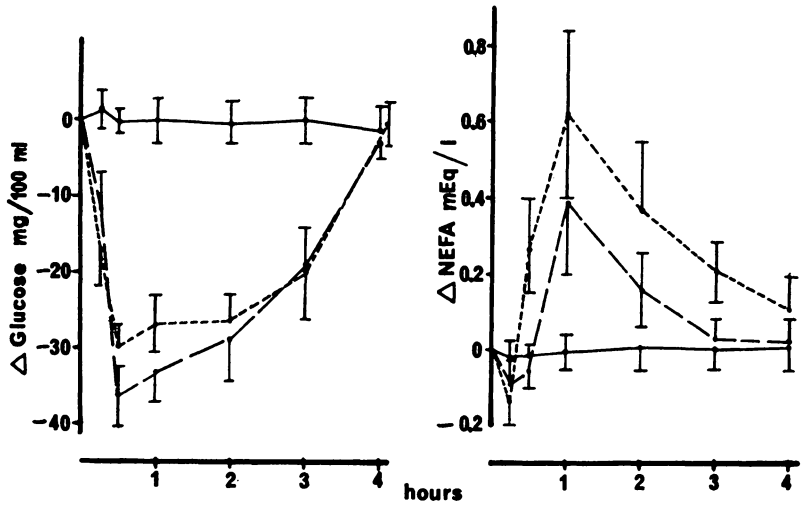

Figure 2. Changes in blood glucose and plasma NEFA in intact ------ and thyroidectomized adult ewes ——— after intravenous injection of 1 i.u./kg of insulin. Intact controls ———. Pretreatment levels were 40±5 mg/100 ml and 0.24±0.06 meq./l in the control group, 42±2 mg/100 ml and 0.28±0.06 meq./l in the intact insulin group and 52±4 mg/100 ml and 0.21±0.05 meq./l in the thyroidectomized insulin group.

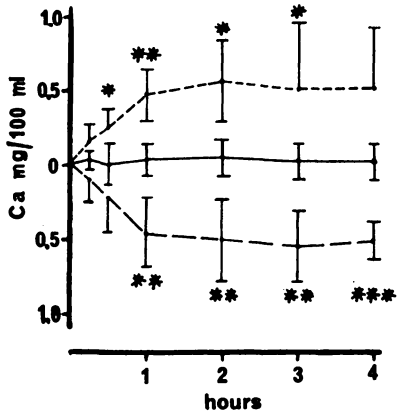

Figure 3. Changes in plasma calcium in intact ------ and thyroidectomized adult ewes ——— after intravenous injection of 1 i.u./kg of insulin. Intact controls ———. Pretreatment level was 9.75±0.64 mg/100 ml in the control group, 9.98±0.70 mg/100 ml in the intact insulin group, and 9.55±0.48 mg/100 ml in the thyroidectomized insulin group.

* $0.05 > P > 0.01$
** $0.01 > P > 0.001$
*** $P < 0.001$

plasma calcium was found (Fig. 3). Apart from the first 2 observations, the difference in calcium response was highly significant throughout the observation period.

The effects of insulin on the plasma levels of inorganic phosphorus and magnesium in intact and thyroidectomized adult ewes are summarized in Table 2. There were no significant changes in the plasma phosphate level in the intact animals, while in the thyroidectomized group a significant reduction was found. Plasma magnesium decreased in both groups.

A statistical comparison between the pretreatment levels of the measured parameters in the thyroidectomized and in the intact animals (control group + intact group receiving insulin, n=12) was made. Blood glucose was 41±4 mg/100 ml in the intact animals and 52±4 mg/100 ml in the thyroidectomized animals. The difference was highly significant ($P < 0.001$). NEFA was 0.26±0.66 meq./l in the intact group and 0.20±0.04 meq./l in the thyroidectomized group. This small difference was almost significant ($0.05 > P > 0.01$). Thyroidectomy did not change plasma calcium significantly. The level was 9.55±0.48 mg/100 ml in the intact animals and 9.86±0.64 mg/100 ml after thyroidectomy. Plasma magnesium was slightly lower in the thyroidectomized group. The levels were 2.44±0.16 mg/100 ml and 2.17±0.30 mg/100 ml respectively. The difference was almost significant ($0.05 > P > 0.01$). Inorganic phosphorus was 4.08±1.08 mg/100 ml in the intact animals and 3.40±0.37 mg/100 ml after thyroidectomy. The difference was not significant.

DISCUSSION

Various effects of insulin on plasma magnesium have been reported. *Rayssiguier & Larvor* (1972) obtained no changes in the magnesium level in rats after insulin shocks, while *Whang et al.* (1966) found decreased plasma magnesium in man after intravenous administration of insulin and glucose. *Aikawa* (1960, 1963) found increased tissue uptake of magnesium in rabbits after insulin treatment. On basis of these results it was suggested that the decrease in plasma magnesium, which sometimes occurs after insulin administration, might be due to increased tissue uptake. In the present study, 0.5 i. u./kg of insulin caused pronounced hypomagnesaemia (Fig. 1).

Infusion of glucose did not alter plasma magnesium (Table 2). If hypomagnesaemia in association with increased glucose

Table 2. The effect of insulin (1 i.u./kg i.v.) on the plasma levels of inorganic phosphorus and magnesium in intact and thyroidectomized ewes. Mean ± s.

	Pretreatment level	Minutes					
		15	30	60	120	180	240
				Δ P mg/100 ml			
Controls (n=6)	3.86±0.84	—0.12±0.39	—0.20±0.38	—0.37±0.64	—0.10±0.34	+0.18±0.24	—0.05±0.17
Insulin, intact animals (n=6)	4.28±1.19	—0.53±0.29	—0.95±1.04	—0.47±0.59	—0.35±0.86	—0.35±0.79	—0.18±0.54
Insulin, thyroidectomized animals (n=6)	3.40±0.37	—0.85±0.19**	—0.97±0.26**	—0.52±0.58	—0.47±0.60	+0.22±0.33	—0.10±0.41
				Δ Mg mg/100 ml			
Controls (n=6)	2.40±0.18	+0.08±0.08	—0.03±0.08	+0.05±0.05	+0.10±0.10	—0.05±0.14	—0.10±0.06
Insulin, intact animals (n=6)	2.48±0.15	+0.02±0.04	—0.12±0.12	—0.28±0.04***	—0.25±0.20**	—0.22±0.12*	—0.13±0.16
Insulin, thyroidectomized animals (n=6)	2.17±0.30	—0.12±0.15*	—0.02±0.19	—0.24±0.13***	—0.07±0.18	+0.02±0.24	+0.02±0.18

* $0.05 > P > 0.01$
** $0.01 > P > 0.001$
*** $P < 0.001$

metabolism is caused by tissue uptake of magnesium as suggested by *Aikawa* (1963) and *Whang et al.*, this would mean that glucose is less effective than insulin in causing a shift of magnesium into the cells.

Catecholamines are strongly glycogenolytic in sheep, and as seen in Table 2 both norepinephrine and epinephrine caused profound and sustained hyperglycaemia. A slight hypomagnesaemia was found after norepinephrine infusion, and also epinephrine reduced plasma magnesium. *Classen et al.* (1971) studied changes in whole blood magnesium in cats after exposure to acute stress. Single injections of epinephrine caused a slight initial decrease in blood magnesium followed by a small rise. A more pronounced elevation of blood magnesium was obtained after infusion of epinephrine, while norepinephrine proved less active. Hypermagnesaemia was also found after withdrawal of blood and asphyxia. In a study in rats, *Larvor* (1968) obtained hypermagnesaemia after epinephrine injection, whereas norepinephrine was without effect. Later *Larvor & Rayssiguier* (1971) showed that pretreatment with phentolamine significantly reduced epinephrine-induced hypermagnesaemia. It was also shown that hypermagnesaemia was not due to increased intestinal absorption or altered urinary excretion. *Gilbert* (1961) had earlier observed in in vitro experiments with frog muscles that a reduction of pH to 2.2 in the incubation medium caused a release of up to 75 % of the intracellular magnesium; when pH was increased to 10.0, magnesium was transported in the opposite direction. Since uncontrolled diabetic acidosis is usually associated with elevated plasma magnesium in spite of increased urinary losses (*Wacker & Parisi* 1968), *Classen et al.* suggested that the stress-producing agents used in their study caused an extracellular acidosis which in turn induced a shift of magnesium from the cells to the extracellular fluid.

The results obtained in the present study showed that sheep differ from rats and cats in magnesium response to catecholamines. The difference can not be explained on basis of the facts obtained. Catecholamines are strongly lipolytic agents, and several authors have reported that calcium is taken up in large amounts in adipose tissue during stimulated lipolysis (*Akgün & Rudman* 1969, *Alm et al.* 1970, *Moseley & Axford* 1971). It was earlier observed that norepinephrine caused hypocalcaemia in sheep, and that hypocalcaemia was reduced when the lipolytic

effect of norepinephrine was inhibited by nicotinic acid. This finding suggested a relationship between lipolysis and hypocalcaemia (*Luthman et al.* 1972). Since magnesium ions are necessary for the activation of adenyl cyclase (*Robinson et al.* 1968), it is not impossible that also magnesium is taken up in adipose tissue during stimulated lipolysis, but there is no evidence for this hypothesis. It can however not be excluded that the catecholamines induced extracellular acidosis also in the sheep, but at the same time also the urinary excretion of magnesium increased, so that even hypomagnesaemia developed.

The thyroidectomized animals showed significantly higher pretreatment levels of blood glucose than did the intacts. The more pronounced hypoglycaemia after insulin injection in the thyroidectomized animals might be related to the higher pretreatment level.

Insulin is the only known hormone which possesses a direct antilipolytic effect. When insulin is injected intravenously plasma NEFA decreases initially, thereafter there is often a rise far above the preinjection level. This biphasic NEFA curve is well known after insulin treatment, and the rebound has long been a matter for discussion. Several authors have reported that the secretion of growth hormone is increased during insulin-induced hypoglycaemia (*Roth et al.* 1963, *Greenwood et al.* 1966, *Croughs et al.* 1968, *Trenkle* 1971). Hypoglycaemia is also a stimulus to increased secretion of catecholamines (*Cier & Klipping* 1956). It thus seems probable that the rebound in NEFA after insulin administration was due to increased secretion of growth hormone and catecholamines, since these hormones are strongly lipolytic in sheep (*Luthman & Jonson* 1972).

NEFA was measured since high NEFA levels sometimes are associated with hypocalcaemia (*Akgün & Rudman, Luthman et al.*). These authors reported that heavy lipolysis is required to produce a fall in plasma calcium (NEFA levels of about 3 meq./l) and as seen in Fig. 2 the maximum rise was less than 1 meq./l.

Hypothyroid subjects are known to show decreased responsiveness to lipolytic stimuli which is in agreement with the results obtained in the present study (Fig. 2). *Krishna et al.* (1968) found adipose tissue from hypothyroid rats to be hyporesponsive to norepinephrine. They proposed that the amount of adenyl cyclase in adipose tissue was reduced by thyroidectomy.

Thyroidectomy did not influence the plasma level of phosphate, which is in contrast to an earlier report (*Luthman & Persson* 1974), where a reduction was found in young sheep. Adult ewes were however used in the present study, and the difference in effect of thyroidectomy was probably due to the higher plasma phosphate level in young animals.

A relationship between phosphate and carbohydrate metabolism has been known for many years. Administration of glucose or insulin usually causes hypophosphataemia, and changes in the plasma phosphate level have been taken as an index of peripheral glucose utilization. The knowledge in this field was summarized by *Burt* (1960). Conflicting results were reported by *Puche et al.* (1973), who obtained a rise in inorganic phosphorus in thyroparathyroidectomized rats treated with insulin. In the present study insulin did not change the plasma phosphate level in the intact group, whereas a significant reduction was found in the thyroidectomized animals (Table 2).

Puche et al. found that insulin caused hypercalcaemia in thyroparathyroidectomized rats, while in intact animals no significant changes occurred. The rise in plasma calcium was of the same degree as that seen after treatment with PTH, and simultaneous administration of insulin and PTH changed plasma calcium in an additive fashion. It was also shown that insulin increased the rate of bone resorption in vitro. It was noted that high doses of insulin were necessary to produce these effects on calcium metabolism and this was the reason for raising the dose to 1 i.u./kg in the present study.

It is evident that the calcium response to insulin (Fig. 3) was dependent on the presence of the thyroid gland, since insulin caused hypocalcaemia in the intact animals, whereas hypercalcaemia was obtained in the thyroidectomized animals. It seems reasonable to assume that insulin increased the rate of bone resorption in the same manner as was reported by *Puche et al.* The most probable explanation for the hypocalcaemia seen in the intact animals is that insulin caused a release of calcitonin to such an extent that the bone resorbing effect of the hormone was blocked and even more, a reduction in plasma calcium occurred. Hypoglycaemia is a stimulus to glucagon release, and the effect of glucagon on plasma calcium is well documented. The role of gastro-intestinal hormones in calcium homeostasis has recently been revealed. Most attention has been paid to gastrin, which is

supposed to serve as a primary signal for calcitonin release before calcium is absorbed from the intestine (*Cooper et al.* 1972). Since *Stadil & Rehfeld* (1972) found that hypoglycaemia is a potent stimulus for gastrin secretion, it is possible that also gastrin was involved in the development of hypocalcaemia after insulin treatment.

From the present data it is suggested that insulin stimulates bone resorption in sheep and also, directly or indirectly, stimulates the release of calcitonin. Since high doses of insulin were used, further work is needed to clarify if insulin plays a physiological role in calcium homeostasis.

REFERENCES

Aikawa, J. K.: Effect of glucose and insulin on magnesium metabolism in rabbits. A study with Mg^{28}. Proc. Soc. exp. Biol. (N.Y.) 1960, *103*, 363—366.

Aikawa, J. K.: The role of magnesium in biologic processes. Charles C. Thomas, Publisher. Springfield, Illinois 1963.

Akgün, S. & D. Rudman: Relationships between the mobilization of free fatty acids from adipose tissue, and the concentration of calcium in the extracellular fluid and in the tissue. Endocrinology 1969, *84*, 926—930.

Alm, B., S. Efendic & H. Löw: Effect of lipolytic and antilipolytic agents on the uptake of ^{47}Ca into rat adipose tissue in vitro. Horm. Metab. Res. 1970, *2*, 142—146.

Buckle, R. M., A. D. Care, C. W. Cooper & H. J. Gitelman: The influence of plasma magnesium concentration on parathyroid hormone secretion. J. Endocr. 1968, *42*, 529—534.

Burt, R. L.: Carbohydrate metabolism in pregnancy. Clin. Obstet. Gynec. 1960, *3*, 310—325.

Care, A. D., L. M. Sherwood, J. T. Potts Jr. & G. D. Aurbach: Perfusion of the isolated parathyroid gland of the goat and sheep. Nature (Lond.) 1966, *209*, 55—57.

Cier, J. F. & J. Klipping (1956). Cited by Natelson, S., J. B. Pincus & G. Rannazzisi: Dynamic control of calcium, phosphate, citrate and glucose levels in blood serum. Clin. Chem. 1963, *9*, 31—62.

Classen, H., G. P. Marquardt, M. Späth & K. A. Schumacher: Hypermagnesemia following exposure to acute stress. Pharmacology 1971, *5*, 287—294.

Conte, N., G. Federspil, S. Frezzato, A. Trisotto, C. Scandellari & G. Piemonte: Glucagon effect on plasma Mg concentration. Horm. Metab. Res. 1972, *4*, 48—50.

Cooper, C. W., W. H. Schwesinger, A. M. Mahgoub, D. A. Ontjes, T. G. Gray & P. L. Munson: Regulation of secretion of thyrocalcitonin. *In* Calcium, Parathyroid Hormone and the Calcitonins. Eds. R. V. Talmage & P. L. Munson. Excerpta Medica, Amsterdam 1972.

Croughs, W., W. Schopman & H. A. W. Tiddens: Plasma growth hormone response to insulin-induced hypoglycemia. Helv. paediat. Acta 1968, *23*, 464—477.

Dole, V. P.: A relation between non-esterified fatty acid in plasma and the metabolism of glucose. J. clin. Invest. 1956, *35*, 150—154.

Gilbert, D. L.: Effect of pH on muscle calcium and magnesium. Proc. Soc. exp. Biol. (N.Y.) 1961, *106*, 550—552.

Gill, J. R. Jr., H. B. Bell & F. C. Bartter: Effect of parathyroid extract on magnesium excretion in man. J. appl. Physiol. 1967, *22*, 136—138.

Greenwood, F. C., J. Landon & T. C. B. Stamp: The plasma sugar, free fatty acid, cortisol, and growth hormone response to insulin. I. In control subjects. J. clin. Invest. 1966, *45*, 429—436.

Hanna, S. & I. MacIntyre: The influence of aldosterone on magnesium metabolism. Lancet 1960, *2*, 348—350.

Heaton, F. W.: The parathyroid glands and magnesium metabolism in the rat. Clin. Sci. 1965, *28*, 543—553.

Krishna, G., S. Hynie & B. B. Brodie: Effect of thyroid hormones on adenyl cyclase in adipose tissue and on free fatty acid mobilization. Proc. nat. Acad. Sci. (Wash.) 1968, *59*, 884—889.

Larvor, P.: Effet de l'adrénaline et de la noradrénaline sur la magnésémie et la glycémie du rat. Interference de la dihydroergotamine et de l'insuline. (Effect of epinephrine and norepinephrine on the blood levels of glucose and magnesium in the rat. Influence of dihydroergotamine and insulin). Ann. Biol. anim. 1968, *8*, 461—464.

Larvor, P. & Y. Rayssiguier: Les récepteurs responsables de l'hypermagnésémie consécutive a une injection de catécholamines. (Determination of the receptors responsible for catecholamine-induced hypermagnesemia). Ann. Biol. anim. 1971, *11*, 55—68.

Luthman, J. & G. Jonson: Short-term hormonal effects on blood glucose and non-esterified fatty acids in female sheep. Acta vet. scand. 1972, *13*, 112—127.

Luthman, J. & J. Persson: The hypocalcaemic effect of toluidine blue in sheep. Zbl. Vet.-Med. A. 1974, *21*, 89—95.

Luthman, J., G. Jonson & J. Persson: Studies on norepinephrine-induced hypocalcemia in sheep before and after thyroidectomy. Acta vet. scand. 1972, *13*, 20—30.

Meyer, H. & P. Schmidt: Der Einfluss von Thyroxin auf den Magnesium- und Kalziumstoffwechsel beim Kalb. (The influence of thyroxin on magnesium and calcium metabolism in the calf). Dtsch. tierärztl. Wschr. 1958, *65*, 602—604.

Moseley, G. & R. F. E. Axford: Redistribution of calcium in sheep induced by stress. Proc. Nutr. Soc. 1971, *30*, 58A.

Puche, R. C., M. C. Romano, M. E. Locatto & J. L. Feretti: The effect of insulin on bone resorption. Calcif. Tiss. Res. 1973, *12*, 8—15.

Rayssiguier, Y. & P. Larvor: Hypermagnésémie et sécrétion médullo-surrénalienne. (Hypermagnesemia and secretion of the adrenal medulla). Ann. Biol. anim. 1972, *12*, 479—491.

Robinson, G. A., R. W. Butcher & E. W. Sutherland: Cyclic AMP. Ann. Rev. Biochem. 1968, *37*, 149—174.

Roth, J., S. Glick, R. S. Yalow & S. A. Berson: Hypoglycemia: A potent stimulus to secretion of growth hormone. Science 1963, *140*, 987—988.

Scott, D. & A. Dobson: Aldosterone and the metabolism of magnesium and other minerals in the sheep. Quart. J. exp. Physiol. 1965, *50*, 42—56.

Skerry, D. W.: Di-(2-hydroxy-phenyl-imino)ethane: A new indicator for the EDTA titration of serum calcium. Clin. chim. Acta 1965, *12*, 593—597.

Stadil, F. & J. F. Rehfeld: Hypoglycaemic release of gastrin in man. Scand. J. Gastroent. 1972, *7*, 509—514.

Trenkle, A.: Influence of blood glucose levels on growth hormone secretion in sheep. Proc. Soc. exp. Biol. (N.Y.) 1971, *136*, 51—55.

Wacker, W. E. C. & A. F. Parisi: Magnesium metabolism. New Engl. J. Med. 1968, *278*, 712—717.

Walser, M.: Magnesium metabolism. Ergebn. Physiol. 1967, *59*, 185—296.

Whang, R., D. Wagner & D. Rodgers: The effect of intravenous insulin and glucose on serum Mg and K concentration. Clin. Res. 1966, *14*, 390.

SAMMANFATTNING

Effekten av insulin, glykos och katekolaminer på några blodmineraler hos får.

Intravenös injektion av insulin (0,5 I.U./kg) på får medförde en signifikant hypomagnesemi. Det har tidigare observerats att insulin under vissa betingelser har en hypomagnesemisk effekt och förklaringen anses vara ett ökat vävnadsupptag av magnesium. Glykosinfusion påverkade inte plasmamagnesium, däremot medförde noradrenalin och adrenalin en lindring sänkning. Intravenös injektion av insulin (1 I.U./kg) medförde på intakta får hypokalcemi. Samma dos insulin gav på thyreoidektomerade får en stegring i kalciumkoncentrationen. Hyperkalcemin hos dessa antas bero på att insulin ökar benresorptionen medan hypokalcemin hos de intakta djuren sannolikt beror på en ökad frisättning av endogent kalcitonin i sådan omfattning att insulinets effekt på benresorptionen blockeras. Insulin medförde dessutom hypofosfatemi hos thyreoidektomerade får.

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