Effect of Corticosteroid Excess and of Bilateral Adrenalectomy on Metabolism of Mg^{28}.* (25109)

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There is little evidence indicating a clear and direct relationship between adrenal steroids and metabolism of divalent ions. For magnesium ion, the main route of excretion from the body is *via* the kidneys, once this ion has entered the circulation. In adrenal insufficiency it has been reported(1) that magnesium blood levels are elevated. It would appear that this hypermagnesemia is the result of deficient renal excretion. There is only fragmentary evidence which indicates that as a result of adrenal steroid insufficiency certain magnesium dependent tissue enzymes may become altered and result in specific metabolic derangement. This latter evidence would imply either an altered tissue concentration or an altered tissue state for the magnesium ion (2). There is no work reported which indicates any conclusive relationship (or lack of relationship) between magnesium ion and elevated levels of adrenal cortical steroids in animals. With availability of an isotope of magnesium of suitable half-life, we investigated in rats, whether, when compared to the normal, either hyper or hypo adrenal cortical state altered tissue distribution and plasma disappearance of this isotope following its intravenous administration as a single dose.

Materials and methods. A group of 200 female rats of approximately 200 g were used. Of these animals, 100 were used as normal controls; 65 were given 2 mg hydrocortisone daily for one week and 40 rats were bilaterally adrenalectomized 3 weeks before study and maintained on their usual diet plus glucose-salt-bicarbonate mixture added to their drinking water. Under light ether anesthesia, the normal and steroid treated animals received between 0.2 to 0.3 μc Mg^{28} intravenously *via* a tail vein and were then sacrificed serially over the following 2 or more hours. Blood was immediately drawn from the inferior vena cava, and the total heart, total liver, and sample of skeletal muscle taken for assay. The adrenal insufficient animals were handled in the same way, except that they received no anesthesia.‡ Two ml samples of plasma, the total heart, total skeletal muscle sample, and a 2 ml aliquot of an acid digest of the liver was counted. All data are expressed in terms of concentration of Mg^{28}/ml of plasma or gram of tissue as percent of administered dose of isotope. Total heart and liver weight were determined on the basis of percent of body weight(3). Total muscle samples were weighed and counted in tared stoppered counting tubes. The method of assay, calibration and counting isotope in plasma and tissue were the same as previously described except that in these studies tissue was not dried to constant weight(4).

Results. Fig. 1 A, B, and C show plasma disappearance and uptake of isotopic magnesium by liver, heart, and skeletal muscle in normal rats following a single intravenous injection. The plasma disappearance curve is similar to that noted in dogs(4). At dose levels used in these rats, uptake of isotopic magnesium by liver, heart and skeletal muscle is rapid and is sustained over 2 hours of observation. During period of observation the turnover of isotope is apparently quite slow. Again the striking difference in avidity of heart muscle as compared to skeletal muscle is noted. Uptake of Mg^{28} by livers of these rats/g of tissue) is slightly higher than heart muscle.

In the steroid treated animals no deviation

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‡ Ether anesthesia had no influence on Mg^{28} distribution or dynamics, since a number of normal and steroid treated rats were studied without prior anesthesia and were identical to those which had received anesthesia.

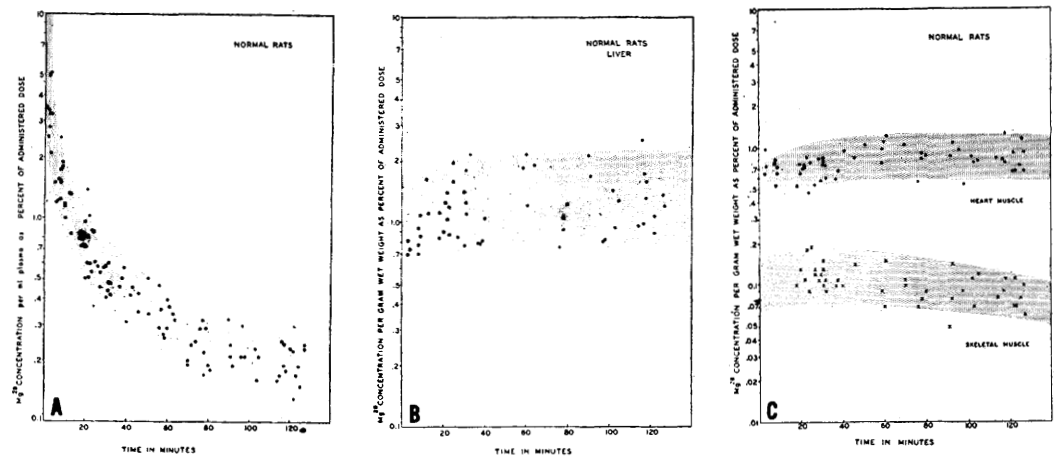

FIG. 1. Normal rats. A. Plasma disappearance of Mg^{28} following a single I.V. inj. B. Uptake of Mg^{28} by liver. C. Uptake of Mg^{28} by heart and skeletal muscle. Shaded areas in A, B and C represent 95% confidence limits for normal data.

from the normal is detectable, as shown in Fig. 2 A, B, C.

No significant deviation from the normal for plasma disappearance of Mg^{28} or its uptake by heart and skeletal muscle is noted in bilaterally adrenalectomized rats (Fig. 3, A, B, C). Uptake of isotope by livers of bilaterally adrenalectomized rats is slow in early periods but reaches normal levels after one hour.

Discussion. For the parameters measured, the data in these normal rats are similar to those obtained in dogs receiving a single intravenous injection of isotopic magnesium. In this respect, the above rat data are merely confirmatory.

With regard to the finding that adrenal steroid excess did not alter plasma disappearance and tissue uptake of Mg^{28} during 2 hours observation, there are 2 possible explanations: (1) at normal steroid levels an optimum effect is already present which additional steroid will not alter and (2) there is no direct relationship between adrenal glucocorticoids and the body's handling of magnesium. In this study we are unable to differentiate definitely between these 2 explanations, both of which appear equally plausible. It would be of interest to study the effects of excess aldosterone on Mg^{28} dynamics since renal loss of magnesium has been reported in cases of primary aldosteronism(5). Apparently from these studies glucocorticoids do not affect the dynamics of the magnesium ion.

With regard to bilaterally adrenalectomized rats maintained without steroid supplementation, no deviation from normal plasma disappearance curve could be detected. In dogs receiving a large single dose of isotopic magnesium intravenously, as much as 30% of administered dose is excreted *via* the kidneys within the first hour(4). Any significant alteration in renal function resulting in inability to excrete magnesium normally as a result of adrenal insufficiency should result in some deviation in magnesium dynamics. In our rats, adrenal insufficiency did not alter the plasma disappearance curve from the normal. This would suggest either that renal excretion was normal or that there must be a higher tissue concentration of the ion to account for the normal plasma curve. Except for a somewhat delayed uptake of Mg^{28} by the liver, tissue concentrations of various soft tissues studied were normal. It may therefore be concluded that in this short term study in rats, adrenal insufficiency in no way altered the dynamics of magnesium disappearance or distribution. Further, if renal function was actually depressed (it was not measured) as a result of adrenal insufficiency, apparently compensation was made here to maintain all measured parameters within normal limits.

It is realized that there is hazard in extra-

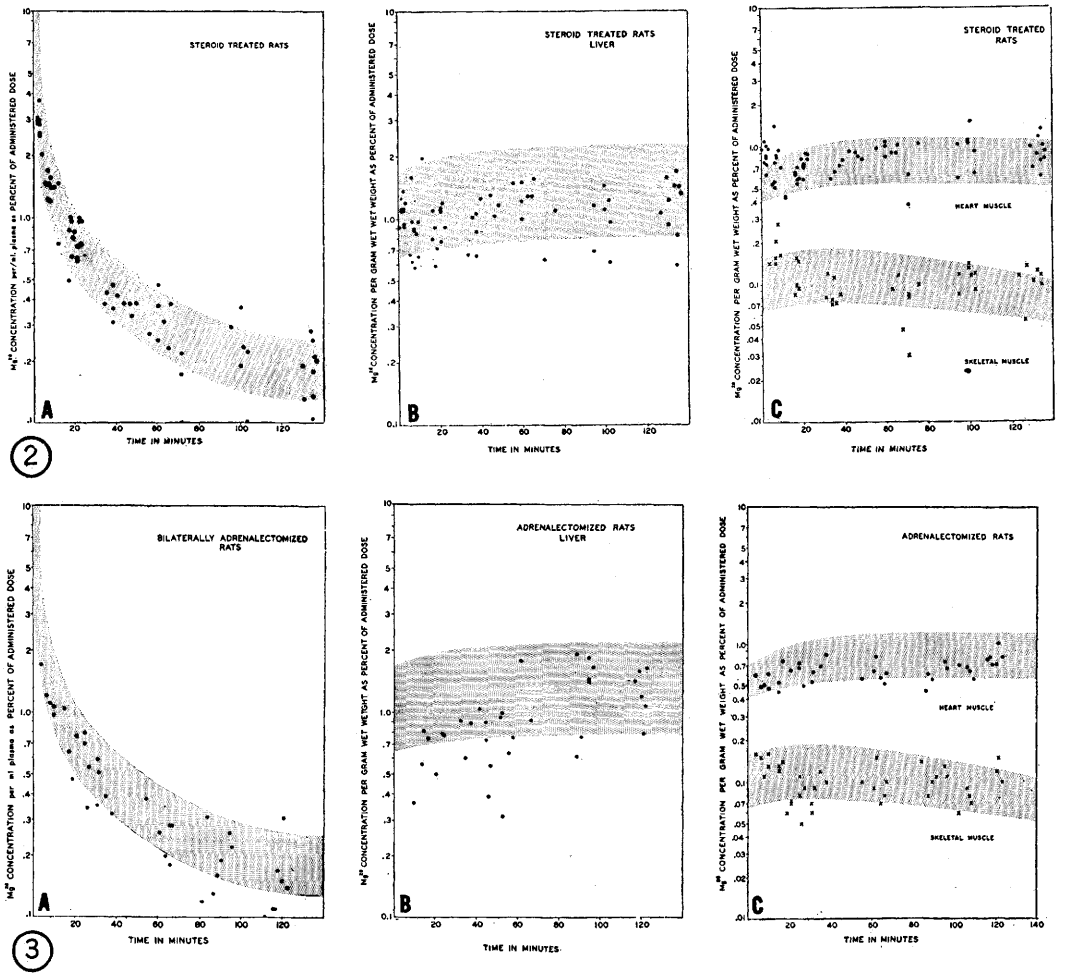

FIG. 2 and 3. Plot of these data is similar to Fig. 1. Shaded area is 95% confidence limit for normal data of Fig. 1.

polating from acute short term studies to long term chronic studies. No statements are warranted from this report relative to chronic experiments which attempt to evaluate effects of long term hyper or hypo-adrenal cortical states to magnesium metabolism. It appears that acutely neither hyper nor hypo-adrenal function alter magnesium metabolism as defined in these studies.

Summary. (1) The plasma disappearance and soft tissue uptake of a single i.v. dose of Mg^{28} was studied in normal rats over a 2 hour period. These results were compared to identical studies in rats given large doses of cortisol and rats made adrenal insufficient. (2) No deviation from normal could be detected in cortisol treated or adrenal insufficient rats.

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