Magnesium Deficiency and Carbohydrate Metabolism

M. E. Kahil, M.D., J. E. Parrish, M.D., E. L. Simons, M.A., and H. Brown, M.D., Houston

SUMMARY

Diet-induced magnesium deficiency in puppies resulted in an increased rate of glucose removal from the blood after intravenous glucose infusions. The levels of immunoassayable insulin in the plasma of these animals were comparable to those of the controls. The accelerated removal of glucose from the plasma was reversed with magnesium treatment. Incubation of intact diaphragms from magnesium-deficient rats demonstrated an increased sugar (2-DG) and amino acid (AIB) uptake from magnesium-free buffer. Although the plasma magnesium concentration rapidly decreased in the deficient rats, a considerably longer period of time elapsed before the changes in sugar transport became apparent. Kinetic studies suggested that the enhanced permeability was due to carrier mediated transport rather than to diffusion. Tissue magnesium levels remained normal despite a significant decrease in the serum magnesium. These studies suggest that some general characteristic of membrane structure and function is affected by the extracellular concentration of magnesium. DIABETES 15:734-39, October, 1966.

The physiological role of magnesium is poorly understood. Because of its relatively high intracellular concentration, its requirement as a cofactor in a number of in vitro biochemical systems, and because of the dramatic syndromes seen in experimental and naturally occurring magnesium deficiency, this cation would appear to play a major role in physiologic processes.

Since many of the biochemical reactions involving magnesium are those of carbohydrate metabolism, it seemed of interest to examine the effects of experimental magnesium deficiency on carbohydrate metabolism in the intact animal. Such studies, to be reported in this paper, demonstrated a striking effect of magnesium deficiency on the peripheral metabolism of glucose. This peripheral metabolism was further examined using in vitro muscle preparations from magnesium-deficient rats and it was found that the penetration of both sugars and amino acids is increased in the magnesium-deficient state. Evidence is also presented to show that this effect is associated with depletion of extracellular magnesium and is readily reversible.

From the Metabolic Research Laboratory, Veterans Administration Hospital, and Department of Medicine, Baylor University College of Medicine, Houston, Texas.

MATERIALS AND METHODS

In vivo studies were carried out on three litters of hound pups approximately seven to nine weeks old. Puppies were used because of the difficulty in producing magnesium deficiency in the adult animal. Each litter was divided into two equal groups and fed a synthetic low magnesium diet* with a magnesium content of 0 to 5 ppm. Thirteen animals, serving as controls, were fed the same diet and received, in addition, 16 mg. per kilogram of body weight per day of magnesium as $MgCl_2$. Distilled water and the diet were given ad libitum to the test animals and the controls were pair-fed. Daily weights and the presence or absence of signs of magnesium deficiency were recorded throughout the experiment. The magnesium content of the serum and red blood cells was determined weekly.[1]

Carbohydrate metabolism was studied in the dogs before and after induction of magnesium deficiency with intravenous glucose, tolbutamide and insulin tolerance tests. All tests were performed after an overnight fast. The glucose tolerance tests were performed weekly by rapidly infusing 0.5 gm. per kilogram of a 20 per cent solution of glucose. Venous bloods for the determination of glucose,[2] nonesterified fatty acids (NEFA),[3] and immunoassayable insulin,[4] were collected in chilled tubes containing sodium fluoride at 0, 1, 5, 10, 15, and 20 min. after the glucose administration. Sodium tolbutamide, 50 mg. per milliliter, was administered intravenously in a dose of 10 mg. per kilogram of body weight. Venous blood samples were collected at 0 and 5 min., and at 1, 2, 4, 6, and 7 hr. after tolbutamide injection. Insulin tolerance tests were performed by measuring the glucose content of blood drawn 30, 45,

*From Nutritional Biochem.

Downloaded from http://diabetesjournals.org/diabetes/article-pdf/15/10/734/340713/15-10-734.pdf by guest on 13 June 2024

60, and 90 min. after the administration of crystalline Zn insulin 0.1 U. per kilogram body weight.

Magnesium deficiency was produced in male rats weighing 115 to 125 gm. by feeding the synthetic low magnesium diet. The control rats were fed the same diet plus 0.27 mEq. of magnesium as $MgCl_2$ daily. At the end of the second week, the animals were killed and intact diaphragms prepared according to the method of Kipnis and Cori.[5]

Unless otherwise specified, the buffer medium was magnesium-free Krebs-Ringer phosphate buffer. The glucose analogue, 2-deoxyglucose (2-DG), was used to assess hexose permeability and phosphorylation. After the intact rat diaphragms were incubated in 30 ml. of buffer containing 0.01 M 2-DG for thirty minutes at 37° C., the hemidiaphragms were quickly excised, blotted, frozen, and weighed. The intracellular content of free 2-DG and 2-deoxyglucose-6-phosphate (2-DG-6-P) was determined as described by Kipnis and Cori[6] except that the colorimetric procedure of Waravdekar and Saslaw for deoxysugars was used.[7] In all of the experiments reported in this study, free 2-DG was not demonstrated intracellularly, and hence the rate of accumulation of 2-DG-6-P was a measure of the rate of 2-DG transport.

Pentose transport was studied with L-arabinose. After incubation, the diaphragms were homogenized and L-arabinose assayed by the p-bromoaniline method of Roe[8] adapted for the Beckman spectrophotometer.

Amino acid transport was studied with the non-metabolizable amino acid analogue α-aminoisobutyric acid-1-C-14 (AIB). Incubations were similar to those described for 2-DG. Following incubation, tissue AIB was extracted with 0.008 N acetic acid and radioactivity measured in a liquid scintillation counter, using internal standards.

Extracellular space, using inulin-C-14, was measured under the same experimental conditions. Intracellular concentration was calculated by the following formula:

$$C_i = \frac{C_t - \left(C_m \times \frac{S_s}{S_w}\right)}{1 - \frac{S_s}{S_w}}$$

where C_i = concentration per ml. intracellular water; C_t = concentration per ml. tissue water; C_m = concentration per ml. incubation medium; S_s = inulin-C-14 distribution in ml. per gram; and S_w = total tissue water in ml. per gram.

RESULTS

Magnesium deficiency syndrome

The characteristic syndrome of magnesium deficiency was produced in all the dogs fed the low magnesium diet. Anorexia and vomiting developed during the third week and there was a slowing of weight gain as compared with that of the controls. By the fifth week, the average cumulative weight gain in the magnesium-deficient and control animals was 2.0 and 3.2 kg., respectively (table 1). Hyperextensibility of the front paws developed in the deficient animals after the third week. Within four to six weeks irritability, ataxia of the hind legs, and convulsive seizures were observed in all the deficient animals.

TABLE 1

Effect of magnesium deficiency on weight gain

Days on experiment	Magnesium-deficient dogs	Control dogs
	Weight in kg. ± SEM	
0	3.4 ± 0.10	3.2 ± 0.18
7	3.9 ± 0.09	3.8 ± 0.33
14	4.5 ± 0.14	4.2 ± 0.48
21	5.0 ± 0.09	4.7 ± 0.50
28	5.0 ± 0.16	5.8 ± 0.39
35	5.4 ± 0.10	6.4 ± 0.34

Serum and erythrocyte magnesium levels

The mean serum and erythrocyte levels of magnesium in the deficient animals fell dramatically after two weeks on the diet from values of 1.88 ± 0.22 and 5.8 ± 0.43 to 0.48 ± 0.04 and 3.8 ± 0.14 mEq. per liter, respectively. An even further fall was observed at four weeks (table 2). Small changes were also observed in the control animals.

TABLE 2

Magnesium concentration in plasma and erythrocytes of dogs

Time on diet	Control diet		Magnesium-deficient diet	
	Plasma	RBC	Plasma	RBC
	mEq./L.			
0	1.85±0.21	5.84±0.36	1.88±0.22	5.84±0.43
2 weeks	1.30±0.06	5.80±0.30	0.48±0.04	3.80±0.14
4 weeks	1.40±0.05	5.20±0.21	0.27±0.02	2.80±0.10

Values represent the mean ± SEM.

Glucose disappearance studies

Intravenous glucose tolerance tests were done prior to and at intervals after beginning the magnesium-deficient diet (figure 1). Prior to the institution of the mag-

Downloaded from http://diabetesjournals.org/diabetes/article-pdf/15/10/734/340713/15-10-734.pdf by guest on 13 June 2024

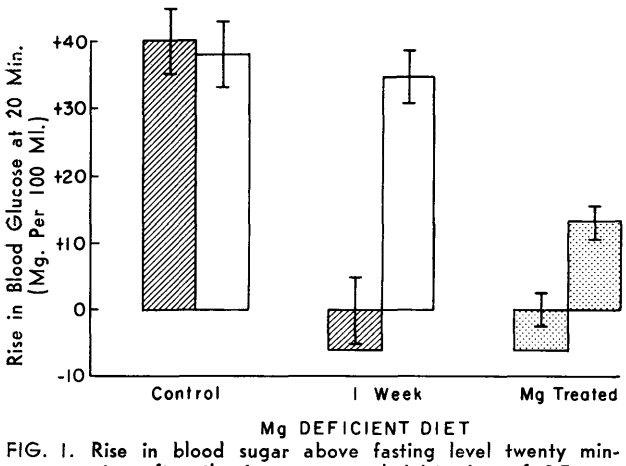

FIG. 1. Rise in blood sugar above fasting level twenty minutes after the intravenous administration of 0.5 gm. glucose per kilogram body weight.

Mg-fed dogs.

Mg-deficient dogs.

Dogs on Mg-deficient diet for one week. Glucose infusion before and sixteen hours after the intramuscular administration of 200 mg. of magnesium.

nesium-deficient diet, 500 mg. per kilogram of glucose administered intravenously to the test and control groups resulted in a mean increment in the plasma glucose level twenty minutes after the glucose infusion of + 39.9 ± 5.1 and + 37.9 ± 4.9 mg. per 100 ml. respectively. After one week on the deficient diet, an acceleration of glucose removal from the blood was evident in the magnesium-deficient animals. The blood glucose excess at twenty minutes was − 6.1 ± 5.1 and + 34.6 ± 4.0 mg. per 100 ml. in the deficient and control dogs, respectively ($P = < 0.001$). This increased glucose disappearance was again observed after two weeks on the diet, the blood glucose variation from initial value being − 2.3 ± 3.5 and + 22.7 ± 2.7 mg. per 100 ml. ($P = < 0.001$) in the magnesium-deficient and magnesium-fed animals, respectively.

The maximal blood glucose values attained during the tests were similar at one minute in both groups of animals. The loss of glucose in the urine during the test was negligible in the two groups of animals as only 14 to 28 mg. was excreted.

Sixteen hours after the intramuscular administration of 200 mg. of magnesium, given as 50 per cent $MgSO_4$, a return of the glucose disappearance to the normal pattern was effected in a group of animals maintained on the deficient diet for one week. The serum magnesium level at this time had risen from 0.8 to 1.4 mEq. per liter.

Plasma insulin levels during the glucose tolerance tests were similar in deficient and control dogs. Plasma NEFA response to the glucose load was found to be identical in the two groups. Following administration of exogenous insulin (0.1 U./kg.) the fall in blood sugar was the same in both groups as was the blood insulin and glucose response to intravenous tolbutamide.

In vitro studies

The effect of magnesium deficiency on hexose metabolism at the tissue level was studied with the glucose analogue, 2-DG, a sugar transported by the glucose transport system and phosphorylated by hexokinase to form 2-DG-6-P, an intermediate that is not further metabolized.[6]

The 2-DG uptake of the intact diaphragms of the magnesium-deficient rats was strikingly increased over that of the magnesium-fed animals, the mean intracellular content of 2-DG-6-P being 6.23 ± 0.40 and 1.91 ± 0.28 uM. per milliliter respectively (table 3). This phenomenon was noted in the diaphragms incubated in medium containing no insulin and to a lesser degree in media containing one mU. of insulin per milliliter. With large amounts of insulin (400 mU./ml.) there was no significant difference in the 2-DG uptake of the diaphragms from the two groups of animals.

TABLE 3

Effect of magnesium deficiency on the penetration and phosphorylation of 2-deoxyglucose in the intact rat diaphragm

Intracellular 2-DG-6-P (uM./ml.)					
No insulin		Insulin 1 mU./ml.		Insulin 400 mU./ml.	
Control	Magnesium-deficient	Control	Magnesium-deficient	Control	Magnesium-deficient
1.91 ± 0.28	6.23 ± 0.40	5.22 ± 0.89	9.65 ± 0.75	8.15 ± 0.50	9.55 ± 0.57
P = < 0.001		< 0.01		< 0.1	

Diaphragms were incubated at 37° C. in 30 ml. of magnesium-free Krebs-Ringer phosphate buffer containing 0.01 M 2-DG with constant oxygenation for thirty minutes. Values represent mean ± SEM of eight to twenty-seven experiments.

Downloaded from http://diabetesjournals.org/diabetes/article-pdf/15/10/734/340713/15-10-734.pdf by guest on 13 June 2024

The increased 2-DG penetration in the diaphragms from the magnesium-deficient animals was reversed by adding physiologic amounts of magnesium to the incubation medium (2.6 mEq./L.) (table 4), but could not be reversed by substituting manganese (0.65 mEq./L.) or strontium (2.6 mEq./L.) for magnesium. However, the presence or absence of magnesium in the medium did not alter 2-DG permeability in the control rat diaphragms. It is apparent, as is seen in table 5, that although the extracellular magnesium concentration is rapidly decreased in the deficient animals, a considerably longer period of time is necessary before the changes in permeability are observed.

TABLE 4

The effect of magnesium on the penetration of 2-deoxyglucose in magnesium-deficient and control rat diaphragms

	Intracellular 2-DG-6-P (uM./ml.)		
	Mg-free Krebs-Ringer PO_4 buffer		Krebs-Ringer PO_4 buffer
Magnesium-deficient	6.24 ± 0.28		3.36 ± 0.63
		P = <0.005	
Controls	3.68 ± 0.70		2.47 ± 0.20
		P = <0.2	

Intact rat diaphragms were incubated at 37° C. in 30 ml. of buffer containing 0.01 M 2-DG without added insulin and with constant oxygenation for thirty minutes. Values represent the mean ± SEM of six to twelve experiments.

TABLE 5

Effect of duration of hypomagnesemia on the rate of 2-deoxyglucose penetration into intact rat diaphragms

Time in days	Intracellular 2-DG-6-P (uM./ml.)	Serum magnesium (mEq./L.)
0	1.91 ± 0.28	1.52 ± 0.06
3	2.50 ± 0.48	0.41 ± 0.07
6	2.78 ± 0.80	0.33 ± 0.03
8	1.88 ± 0.27	0.36 ± 0.03
10	5.40 ± 0.70	0.25 ± 0.02
14	6.23 ± 0.40	0.31 ± 0.03

Intact rat diaphragms were incubated at 37° C. without insulin in 30 ml. of magnesium-free Krebs-Ringer PO_4 buffer containing 0.01 M 2-DG with constant oxygenation for thirty minutes. Values represent the mean ± SEM of four to twenty-one experiments.

The kinetics of the increased 2-DG permeability seen in the magnesium-deficient state were examined by measuring the temperature coefficient (Q_{10}) of penetration. The Q_{10} for penetration in the absence of insulin was approximately 2 in both the magnesium-deficient and control groups.

The effect of magnesium deficiency on amino acid transport in the intact diaphragm was next examined, using AIB as a model (table 6). In the absence of insulin, an intracellular/extracellular concentration ratio of 1.06 was seen in the diaphragms of the magnesium-deficient animals whereas the control ratio was 0.72.

TABLE 6

Effect of magnesium on α-aminoisobutyric acid (AIB) penetration into magnesium-deficient and control rat diaphragms

	$\frac{\text{Intracellular}}{\text{Extracellular}}$ AIB ratio	
	Mg-free Krebs-Ringer PO_4 buffer	Krebs-Ringer PO_4 buffer
Magnesium-deficient	1.06 ± 0.09	0.52 ± 0.04
Controls	0.72 ± 0.05	0.51 ± 0.03
	P = <0.005	

Intact rat diaphragms were incubated in 4.17×10^{-6} M AIB-1-C-14 for sixty minutes with constant oxygenation at 37° C. without insulin. Values represent the mean ± SEM of six to seventeen experiments.

The increased penetration of 2-DG and AIB did not appear to be the result of an increased permeability through free diffusion into the cells. Although the apparent volumes of distribution of L-glucose and L-arabinose exceeded the inulin space, they did not differ significantly in the diaphragms of control and magnesium-deficient animals (table 7).

TABLE 7

Effect of magnesium deficiency on the distribution of inulin C-14, L-arabinose and L-glucose 1-C-14 in intact rat diaphragm

	Control	Magnesium-deficient
	ml./100 gm. wet weight	
Inulin space		
30 minutes*	16.7 ± 0.8	18.3 ± 0.2
90 minutes	17.6 ± 1.5	18.0 ± 1.4
L-arabinose space		
30 minutes	42.4 ± 1.4	37.9 ± 1.1
90 minutes	52.1 ± 2.2	47.4 ± 2.1
L-glucose space		
30 minutes	23.2 ± 0.7	25.1 ± 0.5
90 minutes	28.7 ± 1.1	31.4 ± 0.8

*Incubation time

Diaphragms were incubated at 37° C. under constant oxygenation with medium containing either a mixture of 5.6×10^{-5} M inulin, carboxyl-C-14 and 3.0×10^{-2} M L-arabinose or 1.46×10^{-5} M L-glucose-1-C-14 alone. Values represent the mean ± SEM of four to ten experiments.

Downloaded from http://diabetesjournals.org/diabetes/article-pdf/15/10/734/340713/15-10-734.pdf by guest on 13 June 2024

Tissue magnesium content

After two weeks on the magnesium-deficient diet, the magnesium content of the diaphragm, liver, and skeletal muscle was measured in the rats and in the dogs. Despite a marked reduction in the serum magnesium levels of the deficient animals, the magnesium content of the tissues examined was similar to that of the controls (table 8).

TABLE 8

Magnesium content of tissues

	Dogs		Rats	
	Magnesium deficient*	Controls	Magnesium deficient*	Controls
	mEq./kg. of wet tissue			
Liver	17.4±0.01	16.5±0.75	16.8±0.02	16.8±0.02
Diaphragm	18.6±0.40	18.6±0.04	24.0±0.80	24.2±0.53
Skeletal muscle	18.0±0.90	19.4±0.90	13.7±0.20	14.4±0.23
Pancreas	24.9±0.32	25.4±0.25	—	—
	mEq./L.			
Plasma	0.48±0.04	1.30±0.06	0.31±0.03	1.52±0.06

*Observations after two weeks on deficient diet. Values represent the mean ± SEM of eight to ten animals.

DISCUSSION

An enhanced disposition rate of glucose loads was a consistent finding in the magnesium-deficient dogs and was evident within one week on the deficient diet. This phenomenon was not the consequence of an abnormal increase or persistence of circulating insulin. The comparable reductions in the blood sugars of the magnesium-deficient and control animals following exogenous insulin and tolbutamide challenges gave no evidence of a heightened sensitivity to insulin. Finally the enhanced glucose utilization was reversed by magnesium supplementation.

The finding of an increased penetration of 2-DG in intact rat diaphragms obtained from magnesium-deficient rats suggests that the increased glucose utilization observed in the magnesium-deficient dogs might be related to increased muscle uptake of sugar.

A decrease in the extracellular magnesium concentration was found to exert a profound influence on the penetration of 2-DG in the present study. This effect, noted in the diaphragms obtained from magnesium-deficient rats, was reversed by adding physiologic amounts of magnesium to the incubation medium. It should be pointed out that although the in vitro changes in sugar penetration were related to the extracellular magnesium concentration, an appreciable period of time elapsed after the in vivo induction of hypomagnesemia before changes in sugar transport could be demonstrated. This lag period would suggest that factors other than the extracellular magnesium concentration were necessary to enhance sugar transport.

The mechanisms responsible for the increased permeability of magnesium-deficient diaphragms to 2-DG are obscure. The comparable rate of entry of L-arabinose and L-glucose into the diaphragms of the magnesium-deficient and the control rats suggests that there is no increased permeability through free diffusion of sugars. Moreover, the Q_{10} of 2 for 2-DG penetration observed in the presence of magnesium deficiency, and in the absence of insulin, suggests that the increased penetration was due to an increase in carrier mediated transport. That the consequence of magnesium deficiency on cellular transport is not limited to glucose is demonstrated by the increased penetration of AIB in the diaphragms of magnesium-deficient rats.

Stimulation of sugar and amino acid uptake by muscle cells, recognized as one of the characteristic actions of insulin, was effected by lowering the extracellular concentration of magnesium. Although an insulin-like effect is suggested by these studies, hypomagnesemia, unlike insulin, did not stimulate L-arabinose transport. Furthermore, alterations in Na^+ and K^+ transport occur in magnesium deficiency which do not conform with the anticipated action of insulin on the transport of these cations. Whang and Welt[9] reported that muscle cells from magnesium-deficient rats were unable to maintain an appropriate concentration gradient for potassium between the intracellular and extracellular fluid. Moreover, the erythrocytes of these animals contained a higher concentration of sodium than the controls. The results are the reverse of the effects noted with insulin which causes an accumulation of intracellular K^+[10] and an increased diffusion of Na^+ out of the cells.[11]

The enhancement of penetration of such a diverse group of solutes as sugar, amino acid, and electrolyte by magnesium deficiency would suggest that some general characteristic of membrane structure and function is affected by magnesium.

ACKNOWLEDGMENT

This study was supported by Grants AM-5063 and FR-00134 from the National Institute of Health.

REFERENCES

[1] Schachter, D.: The fluorometric estimation of magnesium in serum and in urine. J. Lab. Clin. Med. 54:763-68, 1959.

Downloaded from http://diabetesjournals.org/diabetes/article-pdf/15/10/734/340713/15-10-734.pdf by guest on 13 June 2024

[2] Nelson, N.: A photometric adaptation of the Somogyi method for the determination of glucose. J. Biol. Chem. *153*: 375-80, 1944.

[3] Duncombe, W. G.: The colorimetric micro-determination of long-chain fatty acids. Biochem. J. *88*:7-10, 1963.

[4] Morgan, C. R., and Lazarow, A.: Immunoassay of insulin: two antibody system. Plasma insulin levels of normal, subdiabetic and diabetic rats. Diabetes *12*:115-26, 1963.

[5] Kipnis, D. M., and Cori, C. F.: Studies of tissue permeability. III. The effect of insulin on pentose uptake by the diaphragm. J. Biol. Chem. *224*:681-93, 1957.

[6] Kipnis, D. M., and Cori, C. F.: Studies of tissue permeability. V. The penetration and phosphorylation of 2-deoxyglucose in the rat diaphragm. J. Biol. Chem. *234*:171-77, 1959.

[7] Waravdekar, V. S., and Saslaw, L. D.: A sensitive colorimetric method for the estimation of 2-deoxy sugars with the use of the malonaldehyde-thio-barbituric acid reaction. J. Biol. Chem. *234*:1945-50, 1959.

[8] Roe, J. H., and Rice, E. W.: A photometric method for the determination of free pentoses in animal tissue. J. Biol. Chem. *173*:507-12, 1948.

[9] Whang, R., and Welt, L. G.: Observations in experimental magnesium depletion. J. Clin. Invest. *42*:305-13, 1963.

[10] Zierler, K. L.: Effect of insulin on potassium efflux from rat muscle in the presence and absence of glucose. Amer. J. Physiol. *198*:1066-70, 1960.

[11] Ungar, G., and Romano, D. V.: Diffusion across rat diaphragm. I. Movement of sodium and potassium; effect of excitation and correlation with protein structure. Biochim. Biophys. Acta *66*:110-17, 1963.

Downloaded from http://diabetesjournals.org/diabetes/article-pdf/15/10/734/340713/15-10-734.pdf by guest on 13 June 2024

Serum Magnesium Levels in the Newborn Child

Blood electrolyte levels are of interest in the newborn period because of the numerous physiological and nutritional transitions necessitated by the act of birth. For many years it has been known that the neonate exhibits a temporary period of hypocalcemia. On occasion symptoms of tetany supervene. Hypocalcemia is more apt to occur in those infants fed a cows' milk formula, a fact which suggests an etiologic role for the high phosphorus content of cows' milk.

The situation with regard to serum magnesium has been studied recently by C. S. Anast (*Pediatrics 33*:969, 1964). The series included seventy-two full-term newborn infants, with sixty-six older children and forty-seven adults included for comparative purposes. Serum magnesium was determined by the Titan yellow method.

For the adults and older children, the mean level of serum magnesium was 1.96 ± 0.24 mg. per 100 ml., a value quite close to that reported by others (E. Wacker and B. Vallee, in *Mineral Metabolism: An Advanced Treatise,* C. L. Comar and F. Bronner, Editors. Academic Press New York, 1964). The over-all average for the newborn infants during the first five days of life was the same, namely 1.92 ± 0.27 mg. per 100 ml. Values for cord blood (forty-one subjects) averaged 1.89 ± 0.26 mg. per 100 ml. The range was from 1.20 to 2.90 mg. per 100 ml. for all subjects. It is known that serum protein levels in the newborn child are lower than in the adult; since about a third of the serum magnesium is bound to protein, the protein levels (which were not measured) could have accounted for this difference.

The newborn subjects were further subdivided on the basis of age (one to five days), and type of feeding (evaporated cows' milk or breast milk). There was no effect ascribable to age during the first five days of life.

However significant differences in serum magnesium levels made their appearance upon a comparison of the two types of feeding. With the exception of the first day of life, the mean serum magnesium concentrations were higher in the breast fed group. These differences were statistically significant on the third and fourth days. On the latter day, for example, the breast fed babies had a mean level of 2.01 ± 0.27 mg. per 100 ml., while that for the formula fed babies was 1.85 ± 0.24 mg.

Serial determinations were made on a number of infants. The trend of serum magnesium was upward in the breast fed group during the first four days of life, and slightly downward in the artificially fed group. None of the infants had symptoms of magnesium deficiency.

Although the difference between the two groups is small, it is in the same direction as that for serum calcium. The author speculates as to the reasons, and invokes that which has been suggested for neonatal hypocalcemia: the high phosphorus content of cows' milk. Although this fluid has three times the magnesium content of breast milk, the disparity in phosphorus content is even greater, the respective phosphorus-magnesium ratios being 7.6 to 1 and 4 to 1.

It is known that large phosphorus loads are associated with both hypocalcemia and hypomagnesiemia (H. A. Salvesen, A. B. Hastings, and J. F. McIntosh, *J. Biol.*

(*Continued on page 748*)