MAGNESIUM CONSERVATION IN THE HUMAN BEING ON A LOW MAGNESIUM DIET [1]

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In recent years the metabolism of various minerals has been studied in humans by providing diets that are completely or relatively deficient in a particular mineral yet satisfactory in all other nutritional requirements. Many observations (1–6) record the application of this technique to problems in calcium metabolism, and more recently sodium (7, 8) and potassium (9–19) have been investigated by similar methods. The earliest animal experiments to our knowledge in magnesium metabolism, using a diet designed to create a specific deficiency of this element, were those reported by Osborne and Mendel (20). However, these authors only achieved a minimum concentration of 0.012 per cent magnesium in their diets for rats. The first comparable studies in humans were reported by Fitzgerald and Fourman (21), who employed a diet low in magnesium and also a cation exchange resin to produce a depletion via the gastrointestinal tract.

The work presented in this report does not attempt to create a magnesium deficiency, but rather determines the efficiency of the body in conserving magnesium while on a magnesium-free diet. The interpretation of previous magnesium balance studies (4, 22–26) has been obscured by large intakes which make it difficult, if not impossible, to evaluate small positive or negative balances. These and other reports (27, 28) are not in agreement in defining the requirements of healthy adults, and consequently, it is necessary to establish the efficiency of the conserving mechanisms present in the body as a clue to the daily magnesium requirements.

METHODS

Subjects. These were four healthy females ranging in age from 21 to 25 years. Their medical history was not significant, and they were in a state of robust health at the time of the study. Participation was voluntary, and their personal association with the laboratory and their interest in the investigation gave us complete confidence in the faithful observance of the dietary restrictions and in the meticulous collection of the specimens. The four subjects were ambulatory throughout the study and continued to be active at secretarial or technical work in a laboratory. Vigorous exercise was prohibited although exercise such as walking was not restricted.

In Case 1 the 18 day balance study was started on the tenth day of her normal 29 day menstrual cycle, and in Case 2 the study was started on the first day of her normal 28 day menstrual cycle.

Diet. A magnesium-free and calcium-low diet was obtained by taking a patented powdered milk product [3] and reconstituting it with water to the following composition: protein, 1.8 per cent; lactose, 14 per cent; butterfat, 6.1 per cent; and approximately 1.2 calories per ml. The low protein content and high caloric value of the reconstituted liquid are noteworthy in contrast to whole milk. This liquid was processed by percolation through a cation exchange resin column prepared in the sodium and potassium cycle in the ratio of two to three, to approximate the proportion of these elements in whole milk. Iron, manganese, iodine, zinc, copper and cobalt were added in trace amounts to the column effluent. The nitrogen content was unaltered by the resin, the calcium content was reduced to 0.2 mM per liter, and the final concentrations of the potassium and sodium were adjusted to 85 and 74 mEq. per liter, respectively. Analysis of the processed dairy product by flame spectrophotometry, by ammonium phosphate precipitation, and by the titan yellow dye technique indicated that the magnesium content is in the order of one part per million (aproximately 0.08 mEq. per liter) or less. Since each of these methods is not entirely satisfactory for the detection of magnesium in the presence of other ions, we have arbitrarily set a value of 0.12 mEq. per liter as the greatest concentration to be expected and as the magnesium content of the liquid diet. In all probability the magnesium content is far less, an impression confirmed by the complete removal of added radioactive magnesium (Mg^{28}) in the upper half of the cation exchange resin column. The details of the production, of the chemical analyses of the diet, and of the biological assay in rats have been reported elsewhere (29).

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[3] Pream, manufactured by the M & N Dietetic Laboratories, Inc., Columbus, Ohio.

Prior to and following the consumption of this liquid diet the subjects were allowed to take *ad lib.* a diet of their choice, provided that the composition of the diet could be determined from standard food tables (30–32). The monotony of the liquid diet was relieved by a limited supply of additional foods that were virtually free of magnesium. The minor contribution of these to the intake was determined from the food tables.

Weight. The subjects were weighed frequently throughout the study in the morning upon arising prior to consuming any food and after voiding. These weights were obtained with the subjects nude or clad in underclothing only.

Balance method. During the first and last metabolic periods in the program of balance study detailed below, the intake of nitrogen and minerals was obtained from standard food tables (30–32) employing estimates made by an experienced dietitian of the weight of the food servings. During the middle metabolic periods, in which the liquid diet was consumed, less than 5 per cent of the intake came from additional foods of negligible magnesium content; consequently, the intake of nitrogen and minerals was precisely known because of the direct analysis of the liquid diet. The balance method employed relied on food tables for obtaining the intake only during the initial and final metabolic periods, and such errors as this may introduce would not affect the data from the periods of liquid diet consumption.

The output in the urine was determined on a daily basis, and the stool output was determined from the analy-

TABLE I

Daily nitrogen and mineral balances of Case 1

(N expressed in Gm.; Na, K, Mg in mEq.)

Day	Period	N	Na	K	Mg	N	Na	K	Mg	N	Na	K	Mg
		Urine				Stool				Total output			
1		13.5	152	126	6.89	1.78	3.1	12.6	22.6	15.3	155	139	29.5
2	I	9.5	147	101	9.84	1.78	3.1	12.6	22.6	11.3	150	113	32.4
3		8.4	111	51	6.00	1.78	3.1	12.6	22.6	10.2	114	63	28.6
4		8.6	134	94	6.12	1.78	3.1	12.6	22.6	10.4	137	107	28.7
5	II	5.0	50	12	3.01	1.45	20.5	15.2	11.4	6.5	71	27	14.4
6		9.9	109	87	2.91	1.45	20.5	15.2	11.4	11.4	129	102	14.3
7		4.6	42	86	1.00	0.79	13.8	9.7	0.28	5.4	55	96	1.28
8	III	5.4	94	89	0.53	0.79	13.8	9.7	0.28	6.2	107	98	0.81
9		3.7	117	40	0.77	0.79	13.8	9.7	0.28	4.5	130	50	1.05
10		6.5	173	100	0.42	0.79	13.8	9.7	0.28	7.3	187	110	0.70
11		4.6	78	60	0.55	0.66	11.9	9.1	0.02	5.3	90	69	0.57
12	IV	5.2	110	80	0.40	0.66	11.9	9.1	0.02	5.9	122	89	0.42
13		5.5	101	78	0.50	0.66	11.9	9.1	0.02	6.2	113	87	0.52
14		5.2	86	86	0.70	0.66	11.9	9.1	0.02	5.9	98	95	0.72
15		9.6	129	86	5.01	0.97	0.96	15.4	17.2	10.6	129	101	22.2
16	V	14.4	119	95	6.32	0.97	0.96	15.4	17.2	15.4	120	111	23.5
17		7.4	87	66	4.91	0.97	0.96	15.4	17.2	8.4	88	81	22.1
18		8.9	100	48	7.83	0.97	0.96	15.4	17.2	9.9	101	63	25.0
		Intake				Balance							
1		14.5	158	99	26	−0.8	+ 3	−40	− 4.0				
2	I	11.8	197	83	25	+0.5	+47	−30	− 7.0				
3		7.1	205	58	17	−3.1	+91	− 5	−12.0				
4		16.5	140	124	50	+6.1	+ 3	+17	+21.0				
5	II	3.9	102	81	0.6	−2.6	+31	+54	−14.0				
6		4.9	125	99	0.7	−6.5	− 4	− 3	−14.0				
7		4.9	125	100	0.9	−2.4	+70	+ 4	− 0.4				
8	III	5.3	125	98	1.1	−0.9	+18	0	+ 0.3				
9		4.1	101	79	0.6	−0.4	−29	+29	− 0.5				
10		4.7	117	91	0.7	−2.6	−70	−19	0.0				
11		4.1	102	84	0.7	−1.2	+12	+15	+ 0.1				
12	IV	4.3	109	88	0.8	−1.6	−13	− 1	+ 0.4				
13		4.8	125	99	0.7	−1.4	+12	+12	+ 0.2				
14		4.8	125	99	0.7	−1.1	+27	+ 4	0.0				
15		17.7	173	111	29	+7.1	+44	+10	+ 7.0				
16	V	19.4	197	90	31	+4.0	+77	−21	+ 7.0				
17		15.6	187	94	26	+7.2	+99	+13	+ 4.0				
18		10.1	166	56	16	+0.2	+65	− 7	− 9.0				

TABLE II

Daily nitrogen and mineral balances of Case 2

(N expressed in Gm.; Na, K, Mg in mEq.)

Day	Period	N	Na	K	Mg	N	Na	K	Mg	N	Na	K	Mg
		Urine				Stool				Total output			
1		10.1	107	56	6.07	1.60	3.4	13.8	13.2	11.7	110	70	19.3
2	I	10.7	137	62	12.78	1.60	3.4	13.8	13.2	12.3	140	76	26.0
3		9.9	196	76	8.56	1.60	3.4	13.8	13.2	11.5	199	90	21.8
4		10.3	214	68	9.99	1.60	3.4	13.8	13.2	11.9	217	82	23.2
5	II	8.9	109	58	5.25	2.10	21.5	19.0	10.6	11.0	131	77	15.9
6		7.3	131	54	1.18	2.10	21.5	19.0	10.6	9.4	153	73	11.8
7		5.9	170	132	1.13	0.56	4.6	6.0	0.04	6.5	175	138	1.17
8	III	6.8	203	123	1.17	0.56	4.6	6.0	0.04	7.4	208	129	1.21
9		5.6	152	109	0.80	0.56	4.6	6.0	0.04	6.2	157	115	0.84
10		5.5	168	99	1.41	0.56	4.6	6.0	0.04	6.1	173	105	1.45
11		5.1	171	100	1.12	0.55	2.4	5.8	0.30	5.7	173	106	1.42
12	IV	5.6	128	121	1.18	0.55	2.4	5.8	0.30	6.2	130	127	1.48
13		4.5	123	120	1.12	0.55	2.4	5.8	0.30	5.1	125	126	1.42
14		4.4	117	107	0.77	0.55	2.4	5.8	0.30	5.0	119	113	1.07
15		6.7	161	76	3.58	0.92	0.89	7.7	5.9	7.6	162	84	9.5
16	V	9.2	177	68	5.07	0.92	0.89	7.7	5.9	10.1	178	76	11.0
17		10.2	131	63	6.35	0.92	0.89	7.7	5.9	11.1	132	71	12.3
18		9.8	103	63	6.70	0.92	0.89	7.7	5.9	10.7	104	71	12.6
		Intake				Balance							
1		7.6	128	48	14	−4.1	+18	−22	− 5.3				
2	I	11.9	144	77	30	−0.4	+ 4	+ 1	+ 4.0				
3		9.1	275	62	21	−2.4	+76	−28	− 0.8				
4		4.3	106	32	9.3	−7.6	−111	−50	−13.9				
5	II	5.7	148	115	0.2	−5.3	+17	+38	−15.7				
6		6.9	180	142	0.7	−2.5	+27	+71	−11.1				
7		6.1	181	139	0.6	−0.4	+ 6	+ 1	− 0.6				
8	III	6.9	180	142	0.7	−0.5	−28	+13	− 0.5				
9		6.0	150	115	0.5	−0.2	− 7	0	− 0.3				
10		5.8	152	117	0.5	−0.3	−21	+12	− 1.0				
11		5.7	150	116	0.4	0.0	−23	+10	− 1.0				
12	IV	5.7	149	117	0.7	−0.5	+19	−10	− 0.8				
13		5.8	149	117	1.0	+0.7	+24	− 9	− 0.4				
14		5.7	148	118	0.7	+0.7	+29	+ 5	− 0.4				
15		9.2	156	70	17	+1.6	− 6	−14	+ 7.5				
16	V	11.6	141	55	18	+1.5	−37	−21	+ 7.0				
17		11.3	151	61	32	+0.2	+19	−10	+19.7				
18		6.0	113	41	10	−4.7	+ 9	−30	− 2.6				

sis of combined two, four, or five day collections as defined by the length of the metabolic periods. Carmine red was not employed to limit the stool periods, and the interpretation of the results is apparent without this technique.

Serum chemistries and electrocardiograms. During the progress of these studies repeated analyses were carried out for serum magnesium, sodium, potassium, chloride, calcium, phosphorus, total protein, A/G ratio, pH and hematocrit. No influence of the artificial dietary routine was discernible in these determinations, and they will not be referred to again.

Repeated electrocardiograms in Cases 1 and 2 likewise were unchanged from their normal patterns by the dietary routine.

Analytical techniques. Stool analyses were carried out as described by Wallace, Holliday, Cushman, and Elkinton (33) whereby an aliquot of an aqueous homogenate is employed for nitrogen analysis (34), and an aliquot is treated with nitric acid for complete extraction of base. This total extraction of base by nitric acid has been validated by others (35), and the sodium and potassium were determined by flame spectrophotometry (36) and the magnesium by the titan yellow dye method (37). The precision of the magnesium assays is satisfactory, giving a coefficient of variation of 2 per cent calculated from 23 replicate stool analyses. The accuracy is less readily documented since the titan yellow dye method is sensitive to unusual concentrations of other ions commonly found in biological material (38,

39). Each general set of conditions must be tested, and we have invariably found less than a 10 per cent difference between known and determined values if certain unusual ionic ratios are excluded. The urine analyses for sodium and potassium were performed on diluted urine by flame spectrophotometry, and the magnesium analyses were completed on samples of urine that were dried, ashed in platinum in a muffle oven at 550° C., and extracted with hydrochloric acid inasmuch as certain substances in fresh urine were noted to have an inconstant effect on the coupling of the magnesium with the titan yellow dye. These analyses coincided with a change in some of the techniques usually employed in the laboratory so that replicate studies by different methods were carried out to confirm their reliability. The precision and accuracy of the chemical techniques as evaluated elsewhere (40) fall well within those of the balance method.

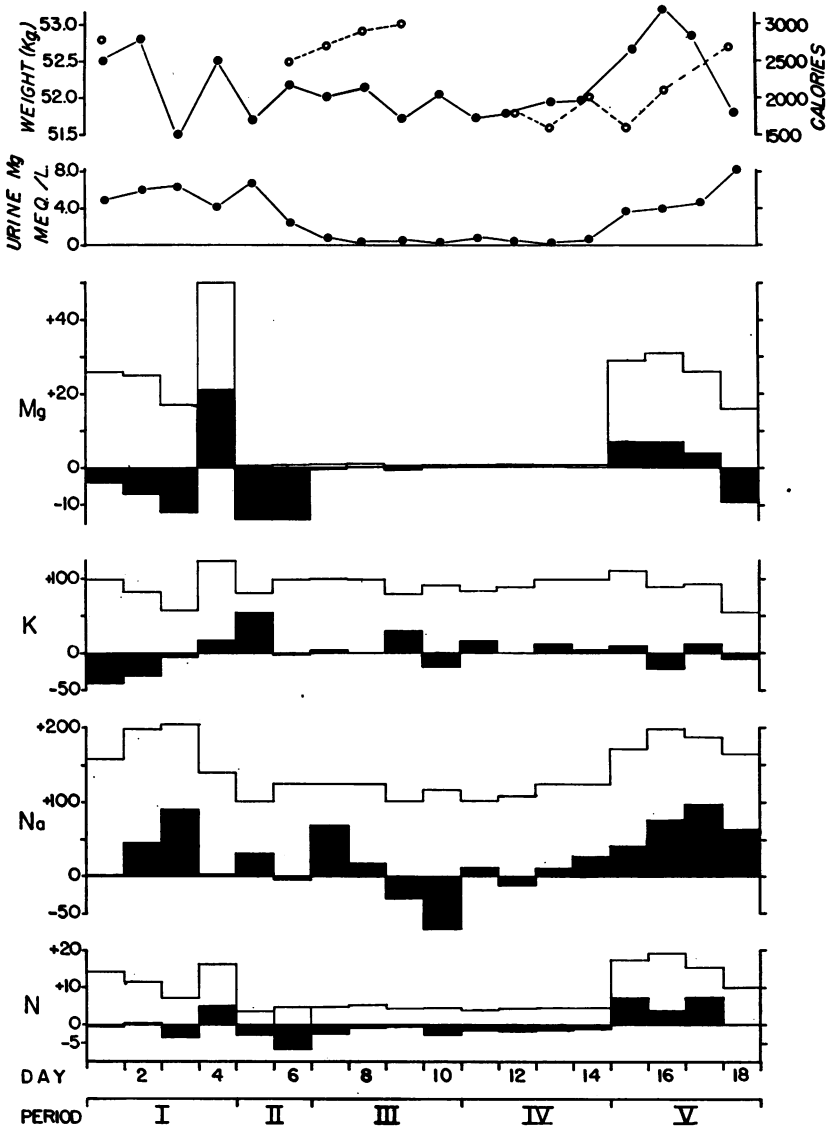

FIG. 1. METABOLIC BALANCE IN CASE 1

The caloric intake is represented by the connected series of solid points, and the available daily weights are represented by circles. In the areas representing the mineral and nitrogen balances the minerals are expressed in mEq. and the nitrogen in Gm. The intake is represented by the line running across the chart above the zero line, and the positive or negative balance is indicated by the solid black area. For the actual values and for the partition of the excretion between the urine and stool, the tables should be consulted.

TABLE III

Daily nitrogen and mineral balances of Case 3

(N expressed in Gm.; Na, K, Mg in mEq.)

Day	Period	N	Na	K	Mg	N	Na	K	Mg	N	Na	K	Mg
		Urine				Stool				Total output			
1		10.7	100	43	5.90	1.49	4.6	11.9	13.7	12.2	105	55	19.6
2	I	11.2	91	54	5.79	1.49	4.6	11.9	13.7	12.7	96	66	19.5
3		11.2	80	54	6.51	1.49	4.6	11.9	13.7	12.7	85	66	20.2
4		17.1	82	50	7.67	1.49	4.6	11.9	13.7	18.6	87	62	21.4
5		8.4	62	63	3.93	0.61	2.8	5.8	0.47	9.0	65	69	4.40
6	II	6.7	130	79	1.77	0.61	2.8	5.8	0.47	7.3	133	85	2.24
7		4.2	74	95	0.39	0.61	2.8	5.8	0.47	4.8	77	101	0.86
8		4.8	101	92	0.36	0.61	2.8	5.8	0.47	5.4	104	98	0.83
9		4.9	116	90	0.32	0.61	2.8	5.8	0.47	5.5	119	96	0.79
10		4.4	123	86	0.38	0.83	4.4	9.1	18.1	5.2	127	95	18.5
11	III	4.3	140	56	2.12	0.83	4.4	9.1	18.1	5.1	144	65	20.2
12		4.7	138	76	5.10	0.83	4.4	9.1	18.1	5.5	142	85	23.2
13		4.6	114	87	6.10	0.83	4.4	9.1	18.1	5.4	118	96	24.2
14		4.1	144	95	6.19	0.83	4.4	9.1	18.1	4.9	148	104	24.3
15		5.6	85	45	8.30	1.23	0.93	9.4	16.6	6.8	86	54	24.9
16	IV	7.4	51	52	6.11	1.23	0.93	9.4	16.6	8.6	52	61	22.7
17		8.6	78	46	4.38	1.23	0.93	9.4	16.6	9.8	79	55	21.0
18		15.4	192	74	7.53	1.23	0.93	9.4	16.6	16.6	193	83	24.1
		Intake				Balance							
1		11.6	54	47	13.7	− 0.6	−51	− 8	− 5.9				
2	I	11.3	76	64	16.9	− 1.4	−20	− 2	− 2.6				
3		16.9	59	95	20.5	+ 4.2	−26	+29	+ 0.3				
4		13.7	64	59	17.1	− 4.9	−23	− 3	− 4.3				
5		5.4	136	103	0.4	− 3.6	+71	+34	− 4.0				
6	II	5.5	136	107	1.1	− 1.8	+ 3	+22	− 1.1				
7		5.1	133	106	0.8	+ 0.3	+56	+ 5	− 0.1				
8		5.5	134	103	0.8	+ 0.1	+30	+ 5	0.0				
9		4.5	117	94	0.8	− 1.0	− 2	− 2	0.0				
10		4.9	119	91	22.3	− 0.3	− 8	− 4	+ 3.8				
11	III	4.9	119	91	22.3	− 0.2	−25	+26	+ 2.1				
12		4.9	119	91	22.0	− 0.6	−23	+ 6	− 1.2				
13		4.5	117	94	22.3	− 0.9	− 1	− 2	− 1.9				
14		3.6	95	73	17.5	− 1.3	−53	−31	− 6.8				
15		16.3	58	93	18.9	+ 9.5	−28	+39	− 6.0				
16	IV	15.8	61	78	20.7	+ 7.2	+ 9	+17	− 2.0				
17		23.1	154	121	31.7	+13.3	+75	+66	+10.7				
18		7.4	71	33	8.9	− 9.2	−122	−50	−15.2				

Program of balance study. Each of the four subjects was placed on an 18 day study. In each case the initial four days were a control period during which time the subjects consumed a simple diet of their own choice. During the next 10 days the liquid diet was consumed, together with a few inconsequential food items and water *ad lib.* At the conclusion of the 10 day period the final 4 days were a control period during which time the subjects again consumed a simple diet of their own choice. The middle 10 days in the first two cases were divided into three metabolic periods: an initial "transitional" 2 day period and two subsequent 4 day periods. The data from these two cases establish a response to a 10 day dietary intake virtually free of magnesium. To avoid confounding the effects of no magnesium intake with that of an artificial, liquid diet the last two subjects had the middle 10 days divided into two 5 day periods. The third subject had approximately 20 mEq. of magnesium per day added to the liquid diet in the second half of the 10 day period, and the fourth subject had this additional magnesium in the first half. The data from these two cases establish the specific effects of magnesium deprivation apart from the experimental routine. Subjects and chemical analysts alike were not aware of the magnesium content of the diet.

RESULTS

The data of the four balance studies are presented in five tables and two charts. Tables I and II present the data from Cases 1 and 2, who were

on the low magnesium diet for 10 days. The low nitrogen content of the diet prevented the subjects maintaining the nitrogen intake at the levels of the first and last metabolic periods. While on the low magnesium diet Case 1 consumed 4.6 Gm. of nitrogen or 29 Gm. of protein a day (0.55 Gm. protein per Kg.). In Case 2 the nitrogen intake averaged 6.0 Gm. or 38 Gm. protein per day (0.50 Gm. protein per Kg.). These intakes are within the range of protein requirements in young adults as determined in the studies of Hegsted, Tsongas, Abbott, and Stare (41) and of Bricker, Mitchell, and Kinsman (42). The minor fluctuations in the magnesium intake are due to the insignificant magnesium content of additional foods permitted during the liquid diet. In both cases following the institution of the low magnesium routine a striking and prompt decrease in the magnesium content of the urine and stool took place. Within two to three days a maximum conservation of magnesium in the urine was achieved, and after the transitional Period II negligible amounts of magnesium appeared in the stool. In the first and fifth periods approximately one-third to one-half of the magnesium output appeared in the urine with the remainder in the stool. Aside from the

TABLE IV

Daily nitrogen and mineral balances of Case 4

(N expressed in Gm.; Na, K, Mg in mEq.)

Day	Period	N	Na	K	Mg	N	Na	K	Mg	N	Na	K	Mg
		Urine				Stool				Total output			
1		15.6	120	51	10.1	1.52	1.92	17.9	15.0	17.2	122	69	25.1
2	I	17.2	118	63	8.78	1.52	1.92	17.9	15.0	18.7	120	81	23.8
3		16.3	146	56	7.87	1.52	1.92	17.9	15.0	18.7	148	74	22.8
4		12.1	62	45	8.13	1.52	1.92	17.9	15.0	13.6	64	63	23.1
5		8.8	116	39	5.98	0.37	3.04	7.3	5.1	9.2	119	46	11.1
6	II	6.0	98	43	2.96	0.37	3.04	7.3	5.1	6.3	101	50	8.1
7		5.4	126	82	4.19	0.37	3.04	7.3	5.1	5.8	129	89	9.3
8		4.0	80	63	3.74	0.37	3.04	7.3	5.1	4.4	83	70	8.8
9		4.6	114	88	5.41	0.37	3.04	7.3	5.1	5.0	117	95	10.5
10		4.9	110	84	3.42	0.69	2.43	14.7	4.2	5.6	113	98	7.6
11	III	4.8	136	67	2.14	0.69	2.43	14.7	4.2	5.5	139	82	6.3
12		5.1	127	86	1.06	0.69	2.43	14.7	4.2	5.8	130	100	5.3
13		5.6	169	78	1.39	0.69	2.43	14.7	4.2	6.3	172	92	5.6
14		4.9	116	100	0.73	0.69	2.43	14.7	4.2	5.6	118	115	4.9
15		5.8	135	59	2.05	0.96	0.72	12.2	5.6	6.8	135	71	7.7
16	IV	10.5	182	66	5.95	0.96	0.72	12.2	5.6	11.4	182	78	11.6
17		9.1	133	37	6.05	0.96	0.72	12.2	5.6	10.1	133	49	11.7
18		10.4	152	77	7.20	0.96	0.72	12.2	5.6	11.4	153	89	12.8
		Intake				Balance							
1		18.6	85	65	20.2	+ 1.4	−37	− 4	− 4.9				
2	I	19.7	101	79	26.5	+ 1.0	−19	− 2	+ 2.7				
3		20.7	81	56	14.6	+ 2.0	−67	−18	− 8.2				
4		12.7	54	59	21.1	− 0.9	−10	− 4	− 2.0				
5		5.1	133	103	24.5	− 4.1	+14	+57	+13.4				
6	II	4.1	100	76	18.5	− 2.2	− 1	+26	+10.4				
7		5.7	138	104	25.0	− 0.1	+ 9	+15	+15.7				
8		4.1	105	82	19.4	− 0.3	+22	+12	+10.6				
9		4.8	114	86	20.9	− 0.2	− 3	− 9	+10.4				
10		4.8	119	95	1.2	− 0.8	+ 6	− 3	− 6.4				
11	III	5.5	136	104	0.9	0.0	− 3	+22	− 5.4				
12		5.7	135	105	0.9	− 0.1	+ 5	+ 5	− 4.4				
13		5.7	138	104	0.7	− 0.6	−34	+12	− 4.9				
14		4.8	120	92	0.5	− 0.8	+ 2	−23	− 4.4				
15		14.7	90	83	19.2	+ 7.9	−45	+12	+11.5				
16	IV	23.2	142	96	28.4	+11.8	−40	+18	+16.8				
17		12.6	81	73	26.3	+ 2.5	−52	+24	+14.6				
18		14.3	139	50	18.6	+ 2.9	−14	−39	+ 5.8				

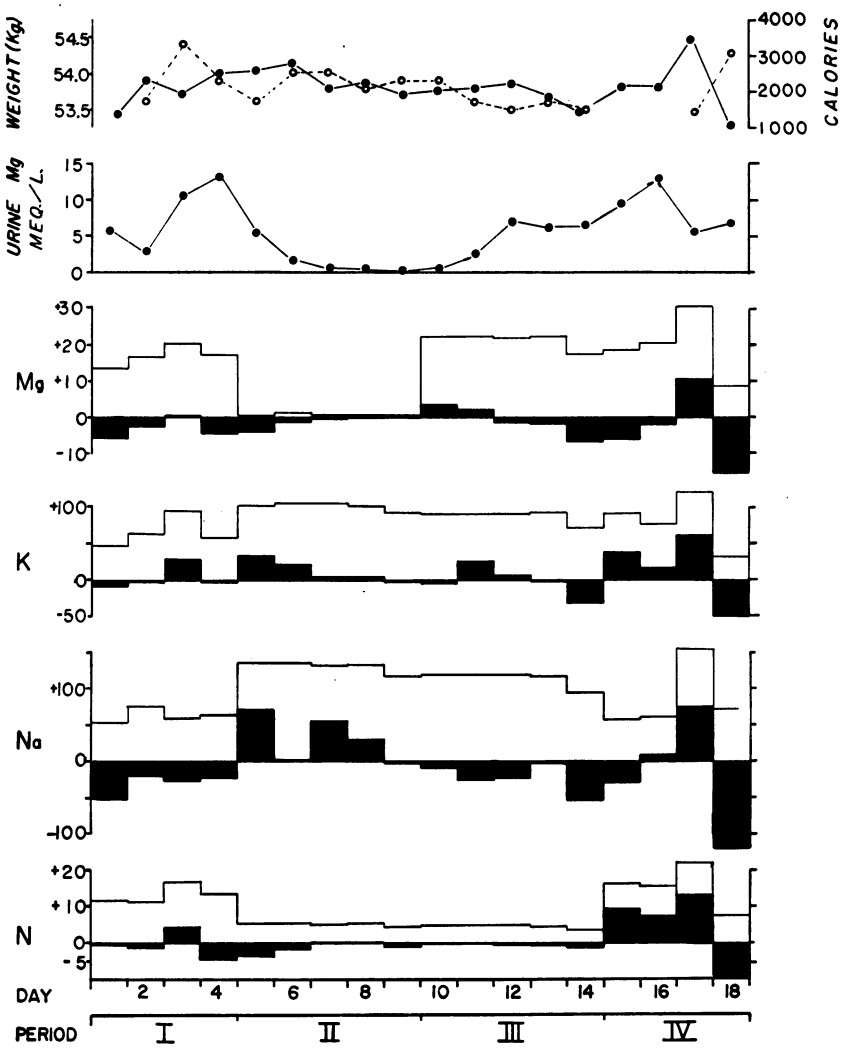

FIG. 2. METABOLIC BALANCE IN CASE 3
Charting convention as in Figure 1.

magnesium changes the balance data do not show any consistent or revealing trends in the other components except for the slightly negative nitrogen balance. This loss is presumably a consequence of the generous nitrogen intake maintained by these subjects normally leading to a release of this element when on a low intake. The urinary conservation of magnesium was less effective in Case 2, but these two studies are in good agreement. The data of Case 1 are charted in Figure 1 where the intake in relation to the balance may be seen. The charting convention employed is similar to that of Moore and Ball (43) and is explained in the legend. The partition of the excretion between the urine and the stool has been omitted for the sake of clarity.

The data of Cases 3 and 4 are presented in Tables III and IV, and they establish the specific effect of a low magnesium intake apart from that of the artificial, liquid diet. A prompt urinary conservation of magnesium appeared more clearly in Case 3 than in Case 4, and it was associated with a marked decline in the stool excretion. The magnesium content of the stools in Case 4 in Period III is a consequence of the carry-over into this period of the residual feces formed while on the high magnesium intake. Aside from the magnesium changes the balance data do not reveal

any consistent trends except for the negative nitrogen balance also seen in the first two cases. Case 3 had a negative magnesium balance throughout the entire study in contrast to Case 4 where a positive balance developed in Periods II and IV when an adequate intake was present. The lag in the stool excretion of magnesium does not appear to account for the positive balances of metabolic Period II. In Figure 2 the data in Case 3 are displayed using the same conventions as explained in the legend of Figure 1.

While on the processed diet the daily calcium intake amounted to 0.3 to 0.5 mM in these four subjects, and prior to this study the dietary habits of the volunteers included the generous calcium intake seen in most urban American diets.

Table V records the serial weights and caloric intakes of the four subjects.

DISCUSSION

This study was directed towards the determination of the magnitude of the obligatory loss of magnesium in normal individuals while on a diet sufficient in other respects. Expect for the study of Fitzgerald and Fourman (21) we are not aware of previous work determining the obligatory magnesium excretion in humans. These authors have reported the application to two humans of an artificial diet with the daily content of 1.1 mEq. of magnesium over a period of three weeks. The effects of this diet were compounded in one subject by the use of a polystyrene sulphonate resin (25 per cent potassium salt and 75 per cent ammonium salt), thereby producing an augmented loss of divalent cations from the gastrointestinal tract. The urinary losses and stool losses of magnesium, apart from those caused by the resin binding of this element, were 1 to 2 mEq. per day, and the total depletion in approximately three weeks was found to be 46 mEq. of magnesium in one subject and 72 mEq. of magnesium in the subject who took the resin. There were no unusual symptoms or signs noted in these individuals at the conclusion of the study.

A feature of the present study is the low nitrogen and calcium intake while on the magnesium-free routine. Therefore, more correctly the results are concerned with the ability of healthy, young, female adults to conserve magnesium while on a normal caloric intake, low nitrogen intake, and a low calcium intake. It is possible that the intakes of nitrogen and calcium may alter the response of the individual to magnesium deprivation and that the conservation of magnesium would be different with other diets. Previous work in animals (44) demonstrates a possible relation between calcium and magnesium in this regard, and our experience is not extensive enough to test this hypothesis in humans. With these restrictions it is clear that the kidney by means of unknown mechanisms is very sensitive to the magnesium intake and promptly suppresses the urinary

TABLE V

Weight and caloric intake of subjects

Day	Case 1		Case 2		Case 3		Case 4	
	Kg.	Calories	Kg.	Calories	Kg.	Calories	Kg.	Calories
1	52.8	2,590	76.8	1,580		1,400	56.8	2,510
2		2,850		3,230	53.6	2,390	56.5	2,650
3		1,520		1,780	54.4	1,980	56.1	1,870
4		2,610		1,000	53.9	2,520	56.4	2,440
5		1,720	76.0	2,230	53.6	2,600	56.5	2,190
6	52.5	2,230	75.9	2,770	54.0	2,780	56.1	1,800
7	52.7	2,080	76.4	2,870	54.0	2,100	56.4	3,020
8	52.9	2,150	75.9	2,770	53.8	2,210	55.0	1,590
9	53.0	1,730		2,680	53.9	1,950	55.9	2,330
10		2,050		2,580	53.9	2,050	56.1	2,090
11		1,720		2,430	53.6	2,100	56.1	2,330
12	51.8	1,790	75.3	2,460	53.5	2,250	56.5	2,650
13	51.6	1,950	75.1	2,340	53.6	1,860	55.7	2,940
14	52.0	1,950		2,300	53.5	1,430	55.7	2,250
15	51.6	2,650		1,320		2,160	56.4	2,950
16	52.1	3,170		1,660		2,150	56.0	3,600
17		2,830		2,840	53.5	3,450	56.1	2,380
18	52.7	1,800	74.4	1,060	54.3	1,120	55.9	2,530

loss when the intake drops to minimal levels. The analytical techniques for serum magnesium are not sufficiently precise today to define slight fluctuations in the serum magnesium that may play a role in the initiation of the conservation. As mentioned previously all the serum chemistries checked during this study were not significantly altered. Furthermore, there is no significant obligatory loss of magnesium in the stool. It is of interest to recall that the normal volume of gastrointestinal juices of 7 to 9 liters a day would deliver to the lumen of the bowel approximately 14 to 18 mEq. of magnesium. This is notably greater than the daily stool loss of magnesium seen in Cases 1 and 2. These facts together with the previous study of Fitzgerald and Fourman (21) indicate why a primary magnesium deficiency is not a common syndrome in humans provided the conserving mechanisms are intact.

The retention of magnesium may be compared to that of other cations more extensively studied. In experiments on the calcium excretion of normal individuals on low calcium diets, Bauer, Albright, and Aub (1) noted a loss of 10 mEq. of calcium per day in the feces and 3.2 mEq. per day in the urine. This study was generally accepted as defining an obligatory loss and carried the implication that conservation would be no better on calcium-free diets. Contrariwise, the work of Steggerda and Mitchell (5) and that of Hegsted, Moscoso, and Collazos (6) imply that the previous dietary intake of calcium is an important factor in the response of the body to low calcium intakes and that an apparent obligatory loss of calcium exists only if an individual has been conditioned by high intakes. To our knowledge calcium balances in human beings, employing a dietary routine with a calcium intake of less than 2 mEq. per day, have not been studied. The calcium balances of these and other subjects are a part of more extended observations being made at the present time.

The conservation of sodium in the urine during a low sodium diet has been studied by Leaf and Couter (8). They alternated an intake of a low sodium diet containing 9 mEq. per day with a high sodium diet containing approximately 450 mEq. per day. The low sodium diet did not initiate a prompt decrease in the renal loss of sodium, but within five or six days the renal excretion had diminished to 1 to 2 mEq. per 24 hours. The subjects lost weight at first, and the data demonstrate that the maximum renal conservation of sodium was not achieved until the reserves of extracellular fluid had been moderately depleted. This lag in renal conservation is presumably due to a delayed response of the adrenal glands or its activating mechanisms to sodium restriction.

The conservation of potassium is in some measure tested by balance studies of individuals on low potassium diets (9, 10, 13–15), but these studies did not achieve an insignificant potassium intake or a specific potassium deficiency in the diet so that the results do not afford the best evidence of the ability of the body to conserve this mineral. Evans, Hughes Jones, Milne, and Steiner (16) reported a study of electrolyte excretion during experimental potassium depletion obtained by feeding a subject a cation exchange resin. The daily fecal loss was approximately 25 mEq. due to the binding of potassium, and a net loss from the gastrointestinal tract ensued since the daily oral intake was only 7 mEq. An additional loss of potassium occurred in the urine where over 20 mEq. was being excreted daily in spite of the sizable negative balance. Fourman (17) gave a subject large amounts of a sulfonic acid exchange resin in the ammonium cycle, but this produced such a pronounced acidosis that only rather restricted conclusions may be drawn concerning the conservation of potassium on such a depleting routine. Black and Milne (12) placed two subjects on a low potassium intake by treating milk with a cation exchange resin to reduce the potassium content to 3 mEq. per liter and, incidentally, the magnesium content to 5 mEq. per liter. Over the seven days of observation the daily urinary potassium fell from approximately 50 mEq. to between 10 and 15 mEq. Other components of the diet were present in satisfactory amounts, and this study is a convincing example of a pure potassium depletion. The fact was clearly established that renal potassium conservation was not effective in preventing a potassium deficit developing quite rapidly. Squires and Huth (19), in an abbreviated report of a low potassium diet study, have demonstrated more effective renal conservation of this element with only 5 mEq. per day appearing in the urine on a daily intake of less than 1 mEq. Certain of these studies and other data on

potassium deficiency have been reviewed (18), and the inadequacies of renal potassium conservation are generally recognized.

The magnesium balance studies reported in this paper provide suggestive, but not conclusive, evidence in favor of a considerable revision downward of the magnesium requirements generally postulated for adult maintenance (4, 23, 26–28, 30). If the conserving mechanisms noted to be effective in these studies over a 10 day period were assumed to be permanent, an intake of less than 1 mEq. of magnesium a day would be sufficient for maintenance. However, the short duration of the study and the completeness of the diet in other respects make such speculations concerning the daily requirement of theoretical more than practical significance. The extent of our efforts and of others to achieve a magnesium-free intake demonstrates the slight chance of such a deficiency developing assuming relatively normal gastrointestinal function and a diet that is sufficient in calories and nitrogen.

Any definitive statement of the magnesium requirements should also consider such losses as arise from the skin and its appendages. These have not been determined in this study. If balance techniques were sufficiently precise, the magnesium requirements would be better defined by a method introduced by Leitch (45) in the study of calcium requirements. This approach would determine the regression line of magnesium intake on balance at different intake levels, including "negative" values obtained by the use of resin *per os*. Until such extended investigations are completed, we suspect the daily magnesium requirement of the adult is considerably less than appreciated formerly, and it may be in the vicinity of 1 mEq. The requirements of growth, convalescence, and pregnancy are, of course, a different problem.

SUMMARY

The application of a liquid diet containing less than 0.12 mEq. of magnesium per liter (approximately 1 part per million by weight) to four volunteers permitted a study of the conservation of magnesium by humans over a 10 day period. Renal conservation prevented maximum losses in excess of 1.5 mEq. per day, and on the average less than 1.0 mEq. of magnesium per day was excreted in the urine. Stool excretion of magnesium while on the liquid diet was negligible after a transitional period.

Magnesium, like sodium, is a component of the body than can be rather rigidly conserved in the presence of a specific deficiency. This is in contrast to potassium where an obligatory loss of significance has been established in essentially normal circumstances.

The adult maintenance requirement may approximate 1 mEq. of magnesium per day.

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