SCIENTIFIC SECTION

THE AVAILABILITY OF THE CALCIUM IN CALCIUM LACTATE IN THE HUMAN.

BY FREDERICK W. HEYL AND MERRILL C. HART.

Sherman (1) has shown that calcium equilibrium can be maintained on amounts varying from 0.27 to 0.78 Gm. Ca per 70 Kg. body weight per day. He places the average at 0.45 Gm. In health with a freely chosen diet this quantity is not always present, and in many conditions, characterized by weakened nutritional function, it is frequently below the minimum maintenance requirements. Long continued negative calcium balances are no doubt part of the clinical picture in many chronic subnormal conditions. Again, in many pathological acidotic conditions, (2) characterized by high urinary ammonia and acid, the body appears to be rapidly thrown into a negative calcium balance. This condition clinically is often superimposed upon a previous prolonged negative balance.

Calcium medication is therefore sometimes resorted to, although of late years so much stress has been laid on the value of the fat-soluble vitamins in connection with calcium metabolism that little has been done to learn how the calcium salts themselves function in the matter of calcium balance. However, Sherman and MacLeod (3) found that increasing the fat-soluble vitamin in the diet did not aid in calcium retention in growing rats which were fed a ration consisting of one-sixth whole milk powder and five-sixths whole wheat, whereas the addition of calcium lactate increased the retention. They state that, in view of the large amount of evidence of the presence of a calcification factor in cod-liver oil, "it is somewhat striking to find here such complete success in the promotion of calcification by the addition of calcium to the diet and no appreciable effect of cod-liver oil." They call attention to the effectiveness of simple increase in calcium intake.

There exists a quite general opinion that so far as maintenance is concerned there is little choice among the various salts. This thought may be strengthened by the results of Steenbock, Hart, Sell and Jones (4) who found in experiments with young rats that there was no difference in the availability of calcium lactate, calcium carbonate, calcium phosphate, calcium silicate or calcium sulphate, when fed at certain high levels. They suggest that the acid reaction of the chyme (5) which lends an acidic reaction to a considerable length of the intestine renders the assimilation of the insoluble salts quite possible. The same thought is found in the suggestion that "some" calcium salt is added to the diet as an accessory.

With the recent development of methods for estimating serum calcium, many studies have been made upon the influence exerted upon the blood-calcium level by different calcium salts. Here also, on account of the marked tendency of serum calcium to remain constant despite calcium treatment, little effect has been observed. Where elevations have been noted they have been rather transient and their significance is perhaps of less importance clinically than a corresponding knowledge of calcium retention. Hjort (6) made a comparative study of the effect of calcium chloride, calcium lactate and calcium glycerophosphate and found that when these were administered orally to dogs in amounts equivalent to 0.2727

Gm. CaO per Kg., that they were absorbed rapidly enough to increase the serum-calcium level. On the other hand, insoluble calcium salts were inconsistent in this respect. When calcium lactate was given in lower dosages it simulated the less soluble salts.

Recently Kahn and Roe (7) found that when 5 Gm. of calcium lactate was given orally on each of five days that the blood calcium on the morning of the sixth day had not been elevated. However, by making blood-calcium estimations at hourly periods after the ingestion of this salt, they proved that this value was increased to the extent of 80% and that an elevation above normal was maintained for several hours. Bauer and Ropes (8) obtained increased blood calcium, but the values are of a much lower order. Roe and Kahn (9) found that the rise in blood calcium following the ingestion of solutions of calcium lactate was depressed by the simultaneous ingestion of foods.

The assimilation of calcium lactate is not completely understood, and is perhaps not used clinically in sufficient quantities. Nevertheless, it is the calcium salt which is most frequently employed. It has been reported by Givens and Mendel (10) that it is a "striking fact that 0.34 Gm. calcium oxide per day in 21.7 Gm. skimmed milk, regardless of acid or base, will produce a positive calcium balance, whereas 1 Gm. of calcium oxide in the form of calcium lactate is necessary to the same end." They state that the "relative advantage of the combination in which calcium is fed is thus raised anew."

Bogert and McKittrick (11) established positive calcium balances with doses of 6 Gm. calcium lactate per day in three of four subjects using a four-day test period.

Calcium lactate is used clinically in average doses of 12 grains and in (12) view of the low calcium content (13%) and the other unknown factors in connection with its metabolism, it appeared of fundamental importance to gain some more accurate idea of its utilization. For inasmuch as it has been deemed important to learn the utilization values of many food-stuffs in respect to calcium, so it is of even greater importance for the clinician to learn something of this value for the lactate and other sources of therapeutic calcium.

These experiments were undertaken upon normal subjects who were placed upon a calcium deficient and acidotic diet of bread, coffee, cream, butter, sugar, steak, pork and vegetables. This is a characteristic diet, (13) and tends to the metabolic equilibria upon which is superimposed the clinical condition requiring perhaps calcium medication. This appears a most reasonable basal diet for the purposes of this study.

EXPERIMENTAL.

Five men lived for fifteen days on a fairly uniform, but not monotonous, diet. During a foreperiod of five days, the basal diet, adequate in respect to protein and energy requirements, consisting of steak, potatoes, bread, butter, coffee, lettuce, bananas and cream, supplied about 0.2 Gm. calcium per day and established a decidedly negative balance. During the following ten days, in each of two series of experiments, there was superimposed upon this acidotic diet (1) milk, (2) calcium lactate in solution. The balances for calcium, magnesium and phosphorus were determined in 5-day periods, but all calculations on maintenance requirements are based on the entire 10-day period.

All articles in the diet were analyzed. Butter, milk and cream were from the same dairy. The same cuts of meat were used throughout the experiment. Bread was purchased daily from the same bakery. These dietary constituents were analyzed several times during the course of the experiment to eliminate any possible variation in their mineral content. Coffee was made in a percolator and the water extract used for the analysis. Potatoes were analyzed after being boiled. Distilled water was used entirely for cooking and drinking.

TABLE I.—CALCIUM, MAGNESIUM AND PHOSPHORUS CONTENT OF FOODS USED IN DIETS (PER GM.).

Foods.		Calcium.	Magnesium.	Phosphorus.
Coffee (extract)		0.000303	0.000957	0.001021
Butter		0.000124	0.000010	0.000113
Bread		0.000132	0.000138	0.000750
Cream (per cc.)		0.000878	0.000112	0.000872
Steak		0.000085	0.000287	0.001959
Onions		0.000105	0.000160	0.000306
Potatoes (boiled)		0.000025	0.000139	0.000415
Apple (raw)		0.000054	0.000080	0.000118
Bananas		0.000051	0.000233	0.000266
Milk (per cc.)		0.001320	0.000141	0.001004
Pork Chops		0.000099	0.000197	0.002024
Lettuce		0.000200	0.000142	0.000301
Sugar	*ad lib.*			

Calcium was determined by the McCrudden (14) method. For magnesium the method given in the Official and Tentative Methods of Analysis of the A. O. A. C. was used. Phosphorus was determined by ashing with a mixture of sulphuric and nitric acid, precipitation with ammonium molybdate, and titration of the yellow phospho-molybdate with 0.5 *N* sodium hydroxide. The amount of the precipitating reagent was adjusted to the estimated amount of phosphorus present. When unexpected quantities of the yellow phospho-molybdate were obtained, it was dissolved in alkali and precipitated as magnesium ammonium phosphate and determined gravimetrically by the official method.

The calcium, magnesium and phosphorus content of the foods used are given in Table I. The diets are recorded in Table II.

The 5-day periods are marked off in the feces by the carmine which was taken just before the first meal of each period. Collections were made in weighed pans, in which they were later dried to constant weight with the use of alcohol. Two Gm. of the finely powdered stool was used for analysis. This was ashed at a dull red heat in a platinum dish in the muffle furnace. The platinum dish was washed out quantitatively with hot 0.5 *N* hydrochloric acid and the filtered acid solution used for the determination of calcium and magnesium.

The daily samples of the urine were collected, diluted to 2 liters with water containing 50 cc. of concentrated hydrochloric acid and preserved with toluene. A measured quantity of the urine is evaporated in a platinum dish, ashed and then extracted in a similar manner to the stools.

In Table III is given the daily intake and output of calcium, when upon the calcium deficient basal diet there is superimposed an increment of milk.

The basal experimental diets contained respectively 0.24, 0.285, 0.21, 0.12, 0.17 Gm. calcium per 70 Kg. body weight, with an average of 0.21 Gm. The

TABLE II.—DAILY FOOD INTAKE IN GRAMS.*

Food.	V. W.	E. O.	E. W.	V. Pe and Em.	Ar.
Coffee	18	18	18	27	27
Potatoes	200	250	250	200	300
Bread	160	225	225	150	250
Steak	200	250	250	250	250
Butter	100	100	100	60	125
Cream	90	150**	130	60***	100
Lettuce	50	...	...	...	75
Bananas	150	250	150	250	250
Onions	100	100	100	...	...
Tomatoes	50	100	100	100	...

* Some latitude was allowed to prevent the diet from becoming monotonous. The steak and bananas, for example, were sometimes replaced with pork chops and baked apples containing an equivalent amount of calcium. With these adjustments no difficulty whatever was experienced with constipation. In fact this diet constitutes a typical "business man's diet."

** In the second series the calcium intake of E. O. was decreased chiefly by decreasing the cream intake to 75 cc.

*** In the second series (calcium lactate experiment) V. Pe increased his calcium intake, chiefly by raising cream intake to 100 cc.

daily calcium requirements for maintenance after this deficient period are calculated approximately as follows: 0.85, 0.71, 0.47, 0.60 and 0.76 Gm. calcium per day. Subtracting the intakes of the basal diet, we have the required increments for maintenance, as follows: 0.61, 0.425, 0.26, 0.48 and 0.59 Gm. For the purpose of comparison these values may be stated to be equal to 4.7, 3.3, 2.0, 3.7 and 4.6 Gm. calcium lactate, with an average of 3.6 Gm.

In four of the five trials an appreciable part of the added calcium was excreted by the kidney (4%–15%).

TABLE III.—AVERAGE DAILY INTAKE AND OUTPUT OF CALCIUM.

(Milk Experiments.)

Subject.	Body weight, Kg.	Added Ca, Gm.	Period.	Output (5-day periods). Urine, Gm.	Feces, Gm.	Total, Gm.	Intake per day, Gm.	Balance per day, Gm.	Average balance 10 days, Gm.
V. W.	50		Ca-low	0.72	0.84	1.56	0.176	—0.14	
		0.460	Ca-high	1.17	1.79	2.96	0.638	+0.05	
		0.460	Ca-high	0.99	2.17	3.16	0.638	+0.01	+0.03
E. O.	61		Ca-low	0.37	1.02	1.39	0.246	—0.04	
		0.476	Ca-high	0.54	2.33	2.87	0.722	+0.15	
		0.476	Ca-high	0.59	2.72	3.31	0.722	+0.06	+0.10
E. W.	73		Ca-low	0.59	1.64	2.23	0.224	—0.22	
		0.508	Ca-high	0.33	2.04	2.38	0.732	+0.26	
		0.508	Ca-high	0.47	2.08	2.55	0.732	+0.22	+0.24
V. Pe	89		Ca-low	0.83	0.85	1.68	0.146	—0.18	
		0.571	Ca-high	0.94	2.53	3.47	0.717	+0.02	
		0.571	Ca-high	0.98	3.08	4.06	0.717	—0.09	—0.04
Em	57			0.47	1.20	1.67	0.14	—0.19	
		0.528		0.67	2.38	3.05	0.668	+0.06	
		0.528		0.67	2.50	3.17	0.668	+0.04	+0.05

In Table IV is given the daily intake and output of calcium, when upon the calcium deficient diet there is superimposed an increment of calcium as lactate. The intake of calcium per day per 70 Kg. man varied as follows: 0.17, 0.14, 0.19, 0.22 and 0.23 Gm., with an average of 0.19 Gm. The daily calcium requirements for maintenance calculated are approximately as follows: 1.25, 1.1, 1.6, 1.3 and 1.9 Gm., calcium per day. Subtracting the intakes of the basal diet, we have the required increments for maintenance as follows: 1.08, 0.96, 1.41, 1.08 and 1.67 Gm., which would be supplied by 8.3, 7.39, 10.85, 8.3 and 12.86 Gm. of calcium lactate. The average increment of the five determinations is 9.5 Gm. Using 6.0 Gm. doses, Bogert and McKittrick report 3 positive balances in four trials, but they used a shorter period (4 days) instead of 10 days. Their method is favorable to lower calcium increments.

Of the *increased* ingested calcium (as lactate) 9% left *via* the urine in Em; 11% in V. Pe; 6% in E. O.; 8% in E. C. W; 12% in Ar.

TABLE IV.—AVERAGE DAILY INTAKE AND OUTPUT OF CALCIUM.

(*Calcium Lactate Experiments.*)

Subject.	Body weight, Kg.	Added Ca, Gm.	Period.	Output (5-day periods). Urine, Gm.	Feces, Gm.	Total, Gm.	Intake per day, Gm.	Balance per day, Gm.	Average balance 10 days, Gm.
Em	60	*	Ca-low	0.40	1.53	1.93	0.145	—0.24	
		1.00	Ca-high	0.84	3.64	4.48	1.145	+0.25	
		1.00	Ca-high	0.84	5.43	6.28	1.145	—0.11	+0.07
V. Pe	89		Ca-low	0.77	1.08	1.55	0.181	—0.19	
		1.25	Ca-high	1.56	3.92	5.48	1.431	+0.34	
		1.25	Ca-high	1.40	7.05	8.45	1.431	—0.26	+0.04
E. O.	60		Ca-low	0.36	1.36	1.73	0.164	—0.18	
		1.25	Ca-high	0.68	5.64	6.32	1.414	+0.15	
		1.25	Ca-high	0.80	6.86	7.67	1.414	—0.12	+0.02
E. C. W.	73		Ca-low	0.54	1.83	2.37	0.227	—0.25	
		1.25	Ca-high	1.00	5.78	6.79	1.477	+0.12	
		1.25	Ca-high	1.01	5.63	6.64	1.477	+0.15	+0.13
Ar	60		Ca-low	0.49	0.86	1.35	0.201	—0.23	
		1.50	Ca-high	1.42	5.21	6.63	1.701	+0.38	
		1.50	Ca-high	1.28	8.51	9.79	1.701	—0.25	+0.06

* After a few preliminary determinations, the feedings were made at approximately the required level for maintenance. For example, Em was negative on an increment of 0.75 Gm. as lactate. The lactate was given in a glass of distilled water, in 3 doses between meals, and at night, so that the food interfered with the absorption as little as possible (10 A.M., 3 P.M., 9 P.M.).

In Table IIIA, the effects of the addition of increments of calcium in the form of milk to the deficient diet is noted on the phosphorus balances. In Table IIIB we record the results obtained at the same time in respect to magnesium balances. As has been noted before, such additions lead to positive balances in respect to phosphorus, but the magnesium balances are not to any noticeable degree favorably influenced. The addition of milk increased the urinary, as well as fecal, excretion of calcium and also of magnesium.

TABLE IIIA.—AVERAGE DAILY INTAKE AND OUTPUT OF PHOSPHORUS.

(*Milk Experiments.*)

Subject.	Phosphorus output (5-day periods). Urine, Gm.	Feces, Gm.	Total, Gm.	Average balance, intake per day, Gm.	Balance per day, Gm.	Average balance 10 days, Gm.
V. W.	2.92	0.81	3.73	0.80	+0.05	
	4.10	1.14	5.24	1.15*	+0.10	
	4.16	1.28	5.44	1.15	+0.06	+0.08
E. O.	3.50	1.20	4.70	1.04	+0.10	
	3.75	1.46	5.21	1.33**	+0.29	
	4.22	1.81	6.03	1.38	+0.17	+0.23
E. W.	3.28	1.37	4.65	1.01	+0.07	
	4.42	1.41	5.83	1.32***	+0.15	
	4.45	2.03	6.48	1.37	+0.08	+0.11
V. Pe	4.00	1.18	5.18	0.86	—0.17	
	4.19	2.06	6.25	1.27[x]	+0.02	
	4.62	2.12	6.74	1.27	—0.08	—0.03
Em	3.64	1.41	5.05	0.91	—0.10	
	3.99	1.66	5.65	1.26[xx]	+0.13	
	4.07	1.63	5.70	1.26	+0.12	+0.13

* Increment 0.35 Gm. per day.
** Increment 0.28 Gm. per day.
*** Increment 0.31 Gm. per day.
[x] Increment 0.41 Gm. per day.
[xx] Increment 0.35 Gm. per day.

TABLE IIIB.—AVERAGE DAILY INTAKE AND OUTPUT OF MAGNESIUM.

(*Milk Experiments.*)

Subject.	Magnesium output (5-day periods). Urine, Gm.	Feces, Gm.	Total, Gm.	Average balance, intake per day, Gm.	Balance per day, Gm.	Average balance 10 days, Gm.
V. W.	0.42	0.54	0.96	0.19	0.00	
	0.58	0.68	1.27	0.25	—0.01	
	0.51	0.67	1.18	0.25	+0.01	+0.00
E. O.	0.46	0.73	1.19	0.25	+0.02	
	0.57	0.64	1.22	0.28	+0.03	
	0.51	0.92	1.43	0.31	+0.03	+0.03
E. W.	0.49	0.66	1.15	0.23	±0.00	
	0.67	0.63	1.31	0.26	±0.00	
	0.70	0.80	1.50	0.29	—0.01	—0.007
V. Pe	0.58	0.74	1.32	0.19	—0.07	
	0.61	0.94	1.55	0.26	—0.05	
	0.70	1.10	1.80	0.26	—0.10	—0.07
Em	0.47	0.96	1.43	0.23	—0.06	
	0.52	0.98	1.50	0.25	—0.05	
	0.52	0.93	1.45	0.27	—0.02	—0.03

In Table IVA, the effect of the addition of calcium lactate on the phosphorus balances are tabulated. In Table IVB, the magnesium balances are reported. In respect to phosphorus, it is observed that negative balances are decreased, chiefly by decreasing the urinary output to a greater extent than the fecal calcium is increased.

In respect to magnesium, we note that urinary excretion is decreased but that, nevertheless, in 3 out of 5 cases, the magnesium losses are slightly increased.

TABLE IVA.—AVERAGE DAILY INTAKE AND OUTPUT OF PHOSPHORUS.

(*Calcium Lactate Experiments.*)

Subject.	Phosphorus output (5-day periods). Urine, Gm.	Feces, Gm.	Total, Gm.	Intake per day, Gm.	Balance per day, Gm.	Average balance 10 days, Gm.
Em	3.87	1.56	5.43	0.871	—0.21	
	3.06	1.29	4.35	0.887	+0.01	
	2.91	1.86	4.77	0.913	—0.04	—0.02
V. Pe	4.41	1.30	5.71	0.920	—0.22	
	3.09	1.28	4.37	0.869	—0.01	
	2.72	2.54	5.26	0.911	—0.14	—0.07
E. O.	2.55	1.45	4.00	0.910	—0.11	
	2.59	1.31	3.90	0.846	+0.06	
	2.47	2.07	4.54	0.897	—0.01	+0.02
E. C. W.	3.99	1.36	5.35	0.995	—0.07	
	3.50	1.81	5.31	1.000	—0.06	
	3.09	1.47	4.56	0.964	+0.05	—0.01
Ar	4.30	1.53	5.83	0.941	—0.22	
	3.51	1.52	5.03	0.902	—0.10	
	3.42	1.66	5.08	0.902	—0.11	—0.11

TABLE IVB.—AVERAGE DAILY INTAKE AND OUTPUT OF MAGNESIUM.

(*Calcium Lactate Experiments.*)

Subject.	Magnesium output (5-day periods). Urine, Gm.	Feces, Gm.	Total, Gm.	Intake per day, Gm.	Balance per day, Gm.	Average balance 10 days, Gm.
Em	0.47	1.13	1.60	0.204	—0.11	
	0.49	0.85	1.34	0.219	—0.05	
	0.46	1.19	1.65	0.234	—0.10	—0.08
V. Pe	0.60	0.77	1.37	0.231	—0.04	
	0.58	0.55	1.13	0.200	—0.03	
	0.50	1.09	1.59	0.231	—0.09	—0.06
E. O.	0.42	0.97	1.39	0.241	—0.04	
	0.41	0.88	1.29	0.219	—0.04	
	0.41	1.08	1.49	0.236	—0.06	—0.05
E. C. W.	0.65	0.52	1.17	0.224	—0.01	
	0.63	0.80	1.43	0.229	—0.06	
	0.60	0.69	1.29	0.212	—0.05	—0.05
Ar	0.71	0.97	1.68	0.255	—0.08	
	0.63	0.81	1.44	0.216	—0.07	
	0.57	0.83	1.40	0.216	—0.06	—0.06

CONCLUSIONS.

1. When calcium lactate is superimposed for ten days upon an acidotic calcium-deficient but vitamin-containing diet, a quantity amounting to approximately 9.5 Gm. is required to establish calcium equilibrium. Compared with milk, this represents 2.5 or more times as much calcium as is necessary using the latter.

2. The urinary calcium excretion was markedly increased, about 10% of the calcium increment taking this route of excretion. The same tendency is noted in using milk.

3. The urinary phosphorus excretion was decreased and phosphorus retention secured by the ingestion of calcium lactate. In this diet the original Ca:P ratio was 2:9; and the favorable influence upon phosphorus metabolism may be due to the establishment of a more favorable balance of 14:9. However, in the case of milk experiments, a ratio of 5:9 yielded a more decided phosphorus retention.

4. Concerning the effect of calcium lactate upon magnesium metabolism, slightly increased losses were noted in three of the five subjects.

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GOLD COMPOUNDS FOR MEDICINAL USE.*

BY F. R. GREENBAUM.

Gold has been used as a drug for many centuries. Abu Moussa Gafar (1) recommended gold in the middle of the eighth century as a remedy for administration to human beings, animals and plants. He believed that all metals were diseased except gold.

Ebu Sina, (2) better known as Avicenna (Arabia, 978–1036), recommended gold, silver and other metals for internal use as blood purifiers. Pills were coated with gold foil and gold paper.

Bombastus Paracelsus (1493–1541), alchemist and chemist, recommended gold

* Scientific Section, A. PH. A., St. Louis meeting, 1927.