STUDIES OF CALCIUM AND PHOSPHORUS METABOLISM [1]: *II. The Calcium Excretion of Normal Individuals on a Low Calcium Diet, also Data on a Case of Pregnancy* [2]

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STUDIES OF CALCIUM AND PHOSPHORUS METABOLISM[1]

II. The Calcium Excretion of Normal Individuals on a Low Calcium Diet, also Data on a Case of Pregnancy[2]

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As a result of the lead studies carried on in this laboratory (1), (2), it has become increasingly apparent that it is important to be able to alter the deposition or mobilization of calcium phosphate in bone. A greater knowledge of the factors which influence calcium balance has therefore been sought. The decision as to the method of approaching this problem involved the following considerations. In the first place it was obvious that very little could be learned by studying the serum calcium alone, as this merely shows the height of the "calcium stream" but gives no indication as to the direction of its flow, into the excretory channels or into the bones. So it at once was clear that analyses of calcium intake and output would be a necessary addition to the blood studies. Furthermore, inasmuch as calcium is excreted into the bowel as well as into the urine, any figure obtained for fecal calcium would consist of two components; the calcium which had passed through the intestines unabsorbed and the calcium which had been absorbed and re-excreted. The latter of these alone can be thought of as actively taking part in the calcium metabolism. A way of overcoming this difficulty would be to have a diet with a calcium intake of zero but adequate in every other respect. Since this is not practicable we adopted a diet with a calcium intake as low

[1] Note:—The title of this series has been changed from Studies of Inorganic Salt Metabolism to Studies of Calcium and Phosphorus Metabolism.

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as possible and still adequate in caloric, protein, and vitamine requirements. By studying the calcium balance of an individual while on such a low calcium intake (about 100 mgm. a day), one can deduce fairly well the rate of endogenous calcium exchange. A further advantage of such a technique is that, by having a very low calcium intake, one largely escapes the many variables which influence calcium *absorption*, such as the acid-base values of the diet (3), the amount of fat (4) (5) or of vitamine D in the diet, and the amount of exposure to ultra violet light. Therefore, a low calcium diet has been used in observing the calcium excretion of normal and pathological individuals, in order to determine factors which caused deviations from the normal. It is the purpose of this paper to present the data for the calcium excretion of some normal people.

NORMAL VARIABLES WHICH INFLUENCE CALCIUM METABOLISM

Other factors which might influence the calcium excretion are (*a*) sex, (*b*) age, (*c*) weight or body surface, (*d*) activity of subject, (*e*) acid-base values of diet, (*f*) amounts of other cations in intake, and (*g*) the phosphorus metabolism.

Sex plays a small but definite part in the quantitative comparison of the energy metabolism. Unless its effects upon calcium metabolism were of a relatively different magnitude it would be insignificant, because the methods available in determining the calcium metabolism are far less precise. In our studies it so happens that our control determinations are all made on men, whereas many of the pathological conditions studied were in women, so that this is a possible source of a small error in our comparisons.

Again, as in energy metabolism, it is not unlikely that age affects in some measure the rate of the calcium metabolism. Of course during the period of bone growth, there must be a marked quantitative effect on the calcium metabolism. In old age the atrophy of bone, as seen by x-ray, suggests a possible alteration in the rate of the calcium metabolism. Aside from these extremes of life, the basal metabolism remains quite constant and it is unlikely that there would be any marked variation in the rate of normal calcium exchange. Our control subjects varied between 19 years and 60 years with an average age of 41.3 years.

The size of the individual must play some part in the rate of the calcium metabolism. Sherman (6), in an effort to determine the calcium requirement for maintenance in man, found it useful to reduce his figures for the calcium excretion, under various inadequate intakes, to the calcium excretion per seventy kilograms. Possibly the calcium excretion per unit of surface area would be theoretically more correct, but we have followed the lead of Sherman and have reduced our calcium excretions and negative calcium balances in our controls to the amount per kilogram of body weight. However, for comparative purposes, we use the figures for the average calcium excretion per person per three day period without reference to weight, and then give the average weight of the control subjects.

As regards the activity of the subject and its effect on calcium metabolism, there is little known. In bone the phenomenon of atrophy of disuse is a very striking and real one, but as far as we know there have been no experiments to show whether this represents an altered calcium metabolism throughout, or merely in the immobilized parts of the body. Experiments are being planned to determine this fact. All but two of our controls were patients up and about the hospital ward; these two were doctors doing strenuous hospital work.

The ingestion of mineral acids has been proven to increase the calcium excretion (1) (7) (8) (9) (10) (11). Diets in which the mineral acid elements predominate over the fixed base elements also lead to decalcification (11) (12) (13) (14). Thus Bogert and Kirkpatrick (12) were able to increase the calcium excretion, especially that in the urine, by changing the food allowance of potato (a basic substance) to rice (an acid substance). The literature leads one to believe that an excess of alkali also leads to decalcification (15) (16). The modus operandi here, however, is possibly due chiefly to decreased absorption because of the increased alkalinity of the intestinal contents (3). For comparative studies like our own, therefore, the acid-base balance of the diet should be constant even if not in acid-base equilibrium. We have not attempted to balance each diet in this respect, but have been content to use a very limited number of food substances, believing that, in this way, the acid-base values would be fairly constant. In order to estimate the variation of our diets in this respect we have shown in table 1 and figure 1 the acid and base elements of five diets. Diets A and B are two of the actual diets used by two of the control patients; the patient eating diet A had the highest urinary calcium excretion of any of the control patients, and the patient eating diet B had one of the lowest urinary calcium ex-

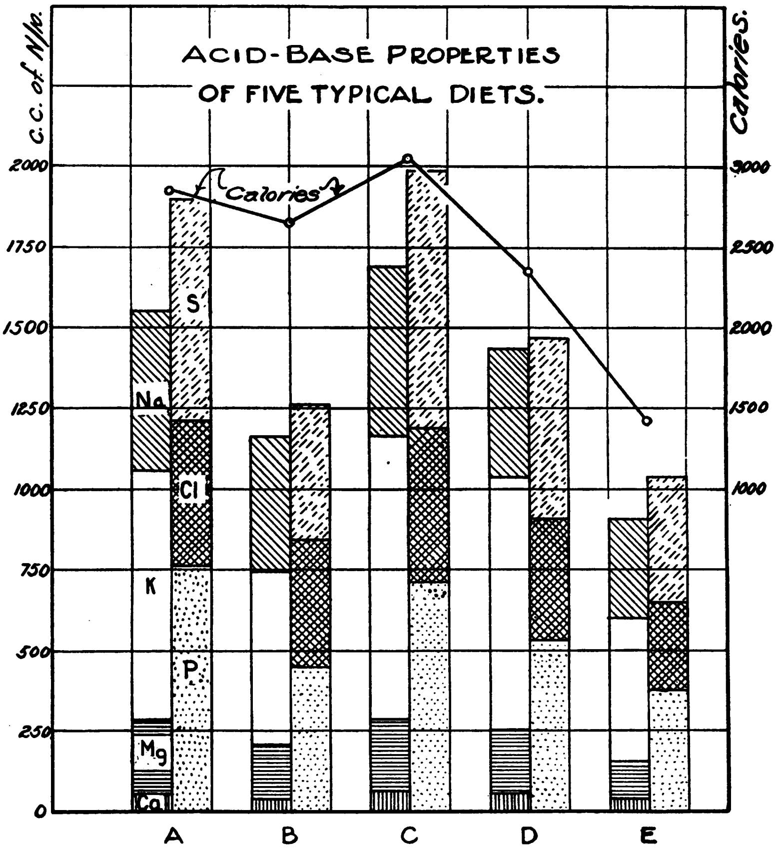

FIG. 1

cretions. Thus it was believed that here, if anywhere, we would find a discrepancy between the acid-base values of the diets.

Diets C, D, and E happen to have been used in later experiments, though they are similar to those used in these controls. The values for the acid and base elements are taken from Sherman and Gettler

(17) and Clark (18). The values in diets C, D, and E, except for sulphur and chlorine, were also checked by actual determination, so that the calculated and actually determined values can be compared. The value of each acid or base element was reduced to cubic centimeters of tenth normal solution, phosphoric acid being considered divalent (17). The total acid value thus obtained was then compared with the total base value and the acid or base balance value noted (see table 1 and figure 1). It will be seen that all five diets

TABLE 1

Acid-base properties of five typical diets†

	Diet A	Diet B	Diet C		Diet D		Diet E	
			Calculated	Found	Calculated	Found	Calculated	Found
Calcium	56	41	66	52	55	43	35	31
Magnesium	230	168	215		196		118	
Potassium	774	533	882		781		446	
Sodium	495	419	525		400		312	
Total base	1,555	1,161	1,688	2,026	1,432	1,647	911	1,223
Phosphorus*	762	453	735	600	530	440	375	369
Chlorine	454	391	453		380		272	
Sulphur	679	424	793		557		387	
Total fixed acid	1,895	1,268	1,981		1,467		1,034	
Excess of acid	340	107	293		35		123	
Calories	2,874	2,660	3,051		2,345		1,421	

* Calculated as divalent.

† All figures in cubic centimeters of N/10, except calories.

had an excess of acid over base—the most acid diet having a net acid value of 340 cc. of tenth normal and the least acid a net acid value of 35 cc. of tenth normal. These variations do not seem excessive. The calculated values agree fairly well with the actually determined values. The total base values actually determined are higher than the calculated ones, due probably to the amount of salt allowed in the diet.[5] The total acid-base metabolism is also

[5] The effect of acid and base excesses in the diet have been thoroughly studied and will be reported in a subsequent paper in this series.

dependent upon the nitrogen balance of the subject, for if the subject is in negative nitrogen balance, one should add to the acid-base values of the ingested food, the acid-base values of the tissue destroyed. Thus in every subject whose calcium metabolism is being determined, one should know the nitrogen balance. This we have done throughout our studies, except in our controls where only two were studied from this aspect. It may be said, however, that the controls were receiving more than a gram of protein per kilo per day, were not losing weight and therefore a negative nitrogen balance, if present, must have been small.

Because of the various inter-relations which the cations, calcium, magnesium, sodium and potassium have (14) (19) (20) (21) (22), in a study of any one of them, it would be desirable that the intakes of all the others be absolutely fixed. To what extent this has been the case in five of our diets can be seen by again referring to table 1 and figure 1.

Calcium metabolism is inseparably linked with phosphorus metabolism. Most of the calcium retained in the body is usually assumed to be in the form of tertiary calcium phosphate deposited in the bones. Phosphoric acid (ingested either as such or as the acid phosphate) produces marked decalcification (11). Neutral sodium phosphate injected into the blood stream also causes an increased calcium excretion (23). So, under ideal conditions, quantitative calcium metabolism studies, if to be used for comparison with other experiments, should have a constant phosphorus intake. We have not attempted to do this but have been content with the variations which our small menu allowed. Table 1 and figure 1 show the actual variation found in five of our diets. As in the discussion of the acid-base values of the diet, it must be pointed out here that unless the subject is in nitrogen equilibrium, the phosphorus in the diet really consists of the phosphorus ingested plus the phosphorus liberated from the destruction of body protein.

EXPERIMENTS

Studies have been made on thirteen individuals. Eleven of these were convalescing from industrial lead poisoning, but were otherwise normal. We have no reason to suppose that lead poisoning affects the rate of calcium metabolism. The other two subjects were doctors doing hospital work. We have in all forty-six three-day periods on these controls. No period was used unless the subject had had a fore period on a low calcium diet (about 100 mgm. a day) of at least 36 hours, or unless at least three days had passed since any medication such as potassium iodide had been used. The details of the prepara-

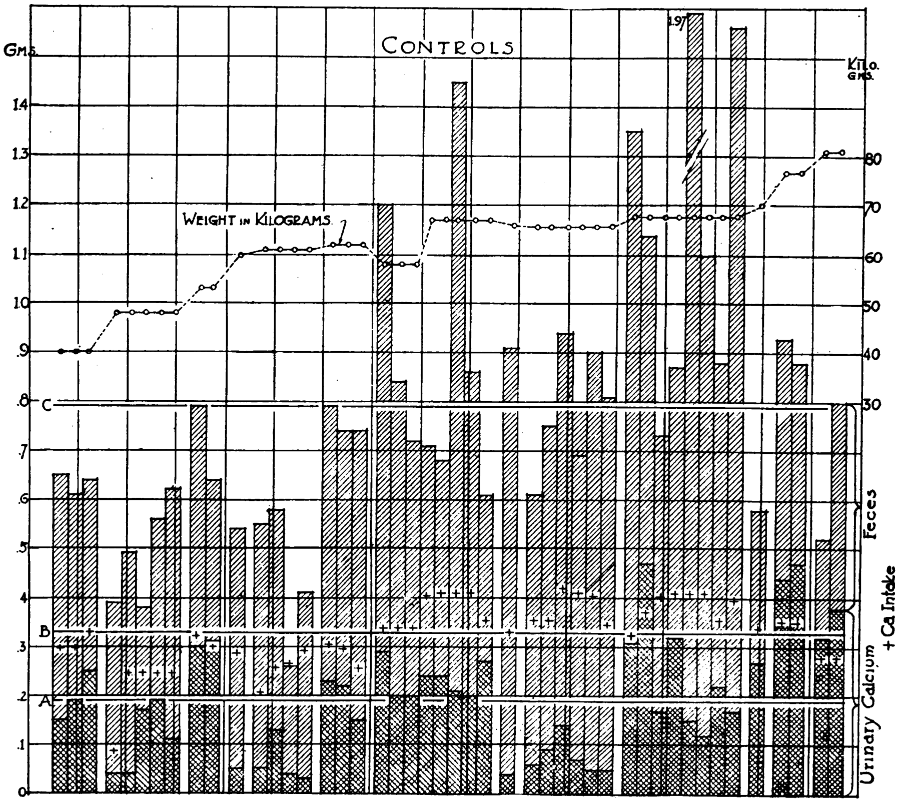

FIG. 2. CALCIUM BALANCE OF 13 CONTROL SUBJECTS ON A LOW CALCIUM DIET

Line *A* represents average urinary calcium excretion; line *B* average calcium intake; line *C* average total calcium excretion. The distance *BC*, therefore, represents the average negative calcium balance.

tion of the diet, the collection of the excreta, and the methods of analysis have been given in a previous paper (24). The data are presented in table 2 and figure 2. The periods from each subject have been grouped together but they are not necessarily consecutive periods. The subjects themselves have been arranged in order of their weights.

TABLE 2

Calcium studies in "normal" controls

Subject	Age	Weight	Period	Calcium in grams per 3-day period: Urine	Feces	Total excretion	Intake	Balance	Total calcium excretion per kilogram	Negative calcium balance per kilogram
		kgm.							*grams*	*grams*
J. P.	60	40	20	0.15	0.50	0.65	0.299	−0.35	0.016	0.0081
			5	0.19	0.42	0.61	0.290	−0.32		
			9	0.25	0.39	0.64	0.336	−0.30		
W. C.	19	48	2	0.04	0.35	0.39	0.085	−0.30	0.010	0.0056
			3	0.04	0.44	0.49	0.246	−0.24		
			4	0.17	0.21	0.38	0.246	−0.13		
			5	0.19	0.37	0.56	0.246	−0.31		
			6	0.11	0.51	0.62	0.246	−0.37		
M. R.	53	53	5	0.30	0.49	0.79	0.322	−0.47	0.013	0.0076
			6	0.31	0.33	0.64	0.300	−0.34		
N. D.	55	60	13	0.05	0.49	0.54	0.288	−0.25	0.009	0.004
K. K.	53	61	6	0.05	0.50	0.55	0.208	−0.34	0.007	0.0032
			7	0.13	0.45	0.58	0.258	−0.32		
			26	0.04	0.22	0.26	0.262	0.0		
			27	0.03	0.38	0.41	0.294	−0.12		
M. C.	50	62	22	0.23	0.56	0.79	0.303	−0.49	0.012	0.0076
			23	0.22	0.52	0.74	0.298	−0.44		
			11	0.15	0.59	0.74	0.252	−0.49		
P. M.	48	58	31	0.29	0.81	1.10	0.340	−0.76	0.014	0.0078
		67	39	0.20	0.65	0.85	0.340	−0.51		
			40	0.20	0.52	0.72	0.340	−0.38		
			63	0.24	0.47	0.71	0.405	−0.31		
			64	0.24	0.44	0.68	0.411	−0.27		
			65	0.21	1.24	1.45	0.411	−1.04		
			66	0.20	0.66	0.86	0.411	−0.45		
			75	0.27	0.44	0.71	0.357	−0.25		
P. S.	39	64	34	0.04	0.86	0.91	0.330	−0.58	0.014	0.0091

TABLE 2—*Continued*

Subject	Age	Weight	Period	Calcium in grams per 3-day period: Urine	Feces	Total excretion	Intake	Balance	Total calcium excretion per kilogram	Negative calcium balance per kilogram
		kgm.							*grams*	*grams*
D. M.	50	66	6	0.06	0.55	0.61	0.355	−0.25	0.012	0.0060
			7	0.09	0.66	0.75	0.355	−0.39		
			14	0.14	0.79	0.93	0.420	−0.51		
			15	0.07	0.62	0.69	0.411	−0.28		
			16	0.05	0.85	0.90	0.405	−0.49		
			17	0.05	0.76	0.81	0.348	−0.46		
J. T.	33	68	9	0.31	1.04	1.35	0.326	−1.01	0.018	0.0119
			18	0.47	0.67	1.14	0.372	−0.77		
			41	0.17	0.56	0.73	0.405	−0.33		
			42	0.32	0.55	0.87	0.411	−0.46		
			43	0.15	1.80	1.95	0.411	−1.54		
			44	0.12	0.98	1.10	0.411	−0.69		
			53	0.22	0.66	0.88	0.357	−0.52		
			59	0.17	1.39	1.56	0.399	−1.16		
J. M.	35	70	2	0.27	0.31	0.58	0.339	−0.24	0.008	0.0034
C. H.	25	77	1	0.44	0.48	0.92	0.35	−0.57	0.012	0.0071
			2	0.47	0.41	0.88	0.35	−0.53		
C. K.	30	81.4	1	0.32	0.20	0.52	0.28	−0.24	0.008	0.0052
			2	0.38	0.46	0.84	0.23	−0.61		
Average....	42.3	67.2		0.19	0.60	0.79	0.33	−0.46	0.012	0.0067

RESULTS

It will be seen from table 2 and figure 2 that there is considerable variation in the calcium excretion not only among different individuals but also among different periods of the same individual. This variation could probably be reduced by a more rigid standardization of the aforementioned normal factors which influence calcium metabolism. However, these figures give us an indication of the amount of calcium which a normal person will excrete on a low calcium diet and their average will be used for future comparisons. Atten-

TABLE 3

Calcium studies on low calcium diets (taken from the literature)

Author	Weight	Calcium in grams per 3-day period					Total calcium excretion per kilogram
		Urine	Feces	Total excretion	Intake	Balance	
	kgm.						*grams*
Von Wendt (36)	71	0.090	0.468	0.558	0.147	−0.411	0.0079
Sherman, Wheeler and Yates (31)	57	0.240	0.600	0.840	0.420	−0.420	
		0.330	0.360	0.690	0.450	−0.240	
		0.360	0.360	0.720	0.420	−0.300	
		0.390	0.270	0.660	0.420	−0.240	
		0.450	0.360	0.810	0.390	−0.420	
		0.390	0.450	0.840	0.390	−0.450	
		0.360	0.330	0.690	0.390	−0.300	
Average		0.360	0.390	0.750	0.411	−0.339	0.0132
Sherman and Winters (32)	54	0.180	0.450	0.630	0.240	−0.390	
		0.150	0.540	0.690	0.240	−0.450	
		0.180	0.540	0.720	0.240	−0.480	
		0.180	0.450	0.630	0.240	−0.390	
		0.270	0.570	0.840	0.600	−0.240	
		0.270	0.750	1.020	0.600	−0.420	
		0.200	0.750	0.950	0.600	−0.350	
		0.300	1.080	1.380	0.990	−0.390	
		0.240	1.020	1.260	0.990	−0.270	
Average		0.219	0.683	0.902	0.527	−0.375	0.0167
Sherman (6)	80	0.330	0.630	0.960	0.690	−0.270	
		0.510	0.450	0.960	0.630	−0.330	
		0.480	0.450	0.930	0.600	−0.330	
		0.540	0.480	1.020	0.630	−0.390	
		0.540	0.480	1.020	0.630	−0.390	
Average		0.480	0.498	0.978	0.636	−0.342	0.0122
Sherman, Wheeler, and Yates (31)	54	0.300	0.750	1.050	0.750	−0.300	
		0.390	0.570	0.960	0.780	−0.180	
		0.420	0.540	0.960	0.780	−0.180	
		0.390	0.570	0.960	0.750	−0.210	
		0.540	0.540	1.080	0.750	−0.330	
		0.570	0.570	1.140	0.750	−0.390	
		0.510	0.600	1.110	0.750	−0.360	
Average		0.446	0.591	1.037	0.759	−0.278	0.0192

TABLE 3—*Continued*

Author	Weight	Calcium in grams per 3-day period					Total calcium excretion per kilogram
		Urine	Feces	Total excretion	Intake	Balance	
	kgm.						*grams*
Rose (37)	45.5	0.174	0.594	0.768	0.846	+0.078	
		0.225	0.375	0.600	0.759	+0.159	
		0.243	0.651	0.894	0.747	−0.147	
Average		0.214	0.540	0.754	0.784	+0.030	0.0166
Sherman, Gillett, and Pope (30)	50	0.210	0.600	0.810	0.810	0.000	
		0.270	0.840	1.110	0.810	−0.300	
		0.300	0.840	1.140	0.840	−0.300	
		0.360	0.870	1.230	0.810	−0.420	
		0.360	0.810	1.170	0.810	−0.360	
		0.360	0.780	1.140	0.810	−0.330	
		0.360	0.870	1.230	0.840	−0.390	
Average		0.317	0.801	1.118	0.818	−0.300	0.0224
Sherman, Gillett, and Pope (30)	57	0.330	0.660	0.990	0.810	−0.180	
		0.410	0.630	1.040	0.810	−0.230	
		0.410	0.690	1.100	0.840	−0.260	
		0.370	0.450	0.820	0.840	+0.020	
		0.360	0.660	1.020	0.840	−0.180	
		0.370	0.480	0.850	0.840	−0.010	
		0.440	0.570	1.010	0.840	−0.170	
		0.340	0.570	0.910	0.840	−0.070	
Average		0.379	0.589	0.968	0.833	−0.135	0.0170
Sherman, Winters, and Phillips (33)	54	0.125	0.795	0.920	0.570	−0.350	
		0.285	1.065	1.350	0.930	−0.420	
		0.420	0.810	1.230	0.930	−0.300	
		0.330	0.930	1.260	0.930	−0.330	
Average		0.290	0.900	1.190	0.840	−0.350	0.0220
Sherman, Gillett, and Pope (30)	52	0.320	0.840	1.160	0.900	−0.260	
		0.340	0.840	1.180	0.900	−0.280	
		0.390	0.810	1.200	0.870	−0.330	
		0.340	1.170	1.510	0.870	−0.640	
		0.270	0.870	1.140	0.870	−0.270	
		0.260	0.870	1.130	0.870	−0.260	
		0.250	0.570	0.820	0.900	+0.080	
		0.270	0.750	1.020	0.900	−0.120	
		0.260	0.900	1.160	0.900	−0.260	
		0.270	0.750	1.020	0.900	−0.120	
Average		0.297	0.837	1.134	0.888	−0.246	0.0218

TABLE 3—*Continued*

Author	Weight	Calcium in grams per 3-day period					Total calcium excretion per kilogram
		Urine	Feces	Total excretion	Intake	Balance	
	kgm.						*grams*
Rose (37)	48	0.249	0.498	0.747	0.771	+0.024	
		0.186	0.480	0.666	0.963	+0.297	
		0.150	0.390	0.540	0.963	+0.423	
Average................		0.195	0.456	0.651	0.899	+0.248	0.0136
Sherman, Winters, and Phillips (33)	67	0.180	1.170	1.350	0.720	−0.630	
		0.390	0.930	1.320	0.720	−0.600	
		0.315	0.840	1.155	0.720	−0.435	
		0.510	1.125	1.635	1.050	−0.585	
		0.420	1.050	1.470	1.050	−0.420	
		0.450	1.290	1.740	1.050	−0.690	
		0.405	1.050	1.455	1.050	−0.405	
Average................		0.381	1.065	1.446	0.908	−0.538	0.0216
Sherman (6)	69	1.020	0.240	1.260	0.540	−0.720	
		0.840	0.330	1.170	1.170	0.000	
		1.080	0.670	1.750	1.200	−0.550	
Average................		0.980	0.413	1.393	0.970	−0.423	0.0202
Rose (37)	56	0.210	0.792	1.002	1.149	+0.147	
		0.207	0.726	0.933	1.149	+0.216	
		0.207	0.573	0.780	1.149	+0.369	
		0.222	0.861	1.083	0.945	−0.138	
		0.231	0.567	0.798	0.945	+0.147	
		0.219	0.981	1.200	0.945	−0.255	
		0.216	0.660	0.876	0.945	+0.069	
		0.237	0.861	1.098	0.945	−0.153	
Average................		0.218	0.753	0.971	1.021	+0.050	0.0173
Bogert and Kirkpatrick (12)	53	0.447	0.744	1.191	1.023	−0.168	0.0225
Rose (37)	54	0.243	0.870	1.113	1.149	+0.036	
		0.213	0.729	0.942	1.149	+0.207	
		0.207	0.645	0.852	1.149	+0.297	
		0.168	0.801	0.969	1.149	+0.180	
		0.099	0.399	0.498	0.945	+0.447	
		0.135	0.495	0.630	0.945	+0.315	
		0.228	0.708	0.936	0.945	+0.009	
		0.228	0.705	0.933	0.945	+0.012	
		0.180	0.717	0.897	0.945	+0.048	
Average................		0.189	0.674	0.863	1.036	+0.173	0.0160

TABLE 3—*Concluded*

Author	Weight	Calcium in grams per 3-day period					Total calcium excretion per kilogram
		Urine	Feces	Total excretion	Intake	Balance	
	kgm.						*grams*
Sherman (6)	61	0.450	1.260	1.710	1.380	−0.330	
		0.540	1.500	2.040	1.230	−0.810	
		0.600	0.780	1.380	1.230	−0.150	
		0.600	1.020	1.620	1.260	−0.360	
		0.600	0.960	1.560	0.960	−0.600	
		0.600	0.630	1.230	0.960	−0.270	
Average.................		0.565	1.025	1.590	1.170	−0.420	0.0260
Bogert and Kirkpatrick (12)	64	0.306	0.984	1.290	1.185	−0.105	0.0201
Bogert and Kirkpatrick (12)	70	0.393	1.152	1.545	1.185	−0.360	0.0221
Final average............	56.6	0.343	0.710	1.053	0.831	−0.222	0.0185

tion is called to the fact that only one individual was in calcium balance and that individual for only one period. The group had an average intake of 0.33 gram per three days, an average output in the urine of 0.19 gram, in the feces of 0.60 gram, making a total average output of 0.79 gram resulting in an average negative calcium balance of 0.46 gram.

In order to compare our results with other similar experiments taken from the literature, tables 3 and 4 and figure 3 have been constructed. In table 3 are given figures for total calcium studies similar to ours, except that different food substances were used in many cases and that the calcium intakes were usually greater. The subjects here are arranged in order of increasing calcium intake rather than by weight. We have recalculated the figures of these other investigators in order that they may be comparable to our figures, i.e., all figures have been reduced to grams of calcium per individual per three day period. In table 4 are given the data for the calcium excretions of fasting men. These observations differ from those in which the diet is inadequate in calcium only (v. supra) because of the great drain on body tissues. In figure 3 these data from the literature are given in graphic form for comparison with the values from figure 2, the average of which is

TABLE 4

Calcium studies on "fasting men" (taken from the literature)

Author	Weight	Calcium in grams per 3-day period					Total calcium excretion per kilogram	Negative nitrogen balance per 3 days
		Urine	Feces	Total excretion	Intake in water	Balance		
	kgm.						*grams*	*grams*
Benedict (38)	58	1.020	0.000	1.020	0.000	−1.020		31.6
		1.086	0.000	1.086	0.000	−1.086		30.8
		0.950	0.000	0.950	0.000	−0.950		30.7
		0.913	0.000	0.913	0.000	−0.913		30.6
	52	0.957	0.000	0.957	0.000	−0.957		28.1
		0.998	0.000	0.998	0.000	−0.998		25.8
		0.914	0.000	0.914	0.000	−0.914		23.1
	49	0.718	0.000	0.718	0.000	−0.718		23.5
		0.611	0.000	0.611	0.000	−0.611		23.5
	47	0.568	0.000	0.568	0.000	−0.568		22.5
Average..................	52	0.873	0.000	0.873	0.000	−0.873	0.0163	27.0
Cathcart (39)	60	0.552	0.000	0.552	0.000	−0.552		31.0
		0.459	0.000	0.459	0.000	−0.459		25.0
		0.288	0.000	0.288	0.000	−0.288		25.0
Average..................	60	0.433	0.000	0.433	0.000	−0.433	0.0072	27.0
Mueller, Munk, Senator, and Zuntz (40)	57	0.885	0.208	1.093	0.171	−0.922		38.1
		1.070	0.208	1.278	0.171	−1.107		31.7
Average..................	57	0.977	0.208	1.185	0.171	−1.014	0.0208*	35.0
Mueller, Munk, Senator, and Zuntz (40)	60	0.305	0.094	0.399	0.219	−0.180	0.0067	33.2
Final average..............	58	0.769	0.031	0.800	0.035	−0.765	0.0137	28.4

* Weight before fast, used.

TABLE 5

Summary chart

	Number of 3-day periods	Weight	Values for calcium in grams per 3-day period					Total calcium excretion per kilogram	Negative nitrogen balance per 3 days
			Intake	Urine	Feces	Total excretion	Balance		
		kgm.						*grams*	*grams*
Average values of table 2.........	46	67.2	0.33	0.19	0.60	0.79	−0.46	0.0120	—
Average values of table 3.........	100	56.6	0.83	0.35	0.71	1.05	−0.22	0.0185	—
Average values of table 4.........	16	58	0.04	0.77	0.03	0.80	−0.76	0.0137	28.4

represented by the first column at the left in figure 3. A line separates the "fasting men" experiments from the others, as they are not quite comparable. In figure 3, aside from the "fasting men," each of whose

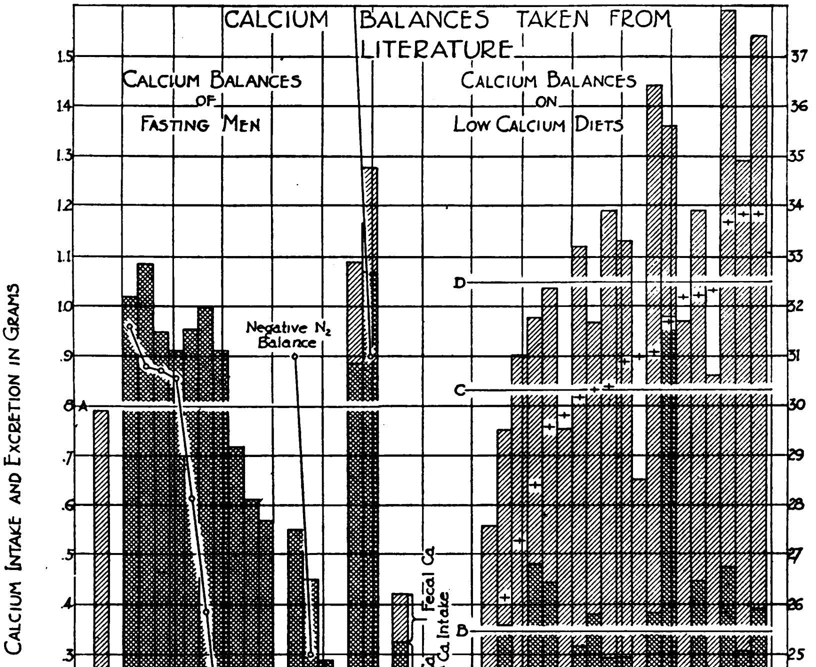

FIG. 3. CALCIUM BALANCES TAKEN FROM LITERATURE

A, Average urinary excretion of "fasting men." *B*, average urinary excretion of persons on a low calcium diet. *C*, average calcium intake. *D*, average total calcium output. Negative nitrogen balances in the "fasting men" are represented thus: o——o

* Graphic representation of average calcium balance from our control series.

three-day periods are charted separately, only the average value for each individual is charted.

In table 5 are given the average values of tables 2, 3, and 4. It will be noted that the urinary calcium excretion is greater in the group from the literature than in our group. This is ascribed to the higher calcium intake. It has been stated that the urinary calcium increases on a low calcium diet (25). This was probably due to some variation in the diet other than the calcium, such as the acid-base value (v. supra). This is borne out by the "fasting men" experiments, whose diet may be thought of as consisting of their own flesh, and therefore very acid. Their average negative nitrogen balance per three days of 28.4 grams would correspond to a calcium content of 0.067 gram (using Katz' figure for calcium value of human flesh) (26). Thus on this very low "intake" of calcium they had a very high average calcium excretion in the urine, 0.767 gram per three-day period.

DISCUSSION

From an inspection of our data and the data collected from the literature it is seen that there is a certain very appreciable minimal requirement of calcium necessary to keep the body in calcium balance. The literature gives abundant proof of this both by experiments on animals (8) (15) (27) (28) and by experiments on people (6) (29) (30) (31) (32) (33). It is this negative calcium balance on a very low calcium intake which we wish especially to emphasize, and the varying degree of which under certain abnormal conditions we intend to make the subject of later papers. We believe that this is an aspect of calcium metabolism which can be quantitatively determined. This appreciable excretion of a necessary body ingredient is not applicable to all body elements. Thus chlorine excretion during starvation sinks to almost zero and a diet deficient in chlorides does not lead to dechlorinization. Of direct interest in this connection are the experiments of Osborne and Mendel (27). These investigators have shown that rats continue to gain weight on diets very low in magnesium, sodium, chlorine or potassium. However, when sodium and potassium were both very low or when either calcium or phosphorus was very low, the rats ceased to gain. Furthermore, an excess of magnesium was without avail in making up for the calcium deficiency. It is their belief that sodium, potassium, magnesium and chlorine can be "husbanded" in the body, but that calcium and phosphorus and at least one of the monovalent cations (sodium or potassium) must be furnished in certain minimal quantities. Likewise Hamilton (28), from calcium balance studies on premature infants, concluded that a certain definite amount of calcium had to be excreted each day regardless of the intake and that only when calcium was furnished in excess of this amount was there a positive balance.

The significance of this negative calcium balance on a low calcium diet can only be speculated on. Hamilton (28) suggests that the calcium may be necessary to neutralize acids. Osborne and Mendel (27) offer a similar explanation for the cessation of growth in their rats on diets very low in both sodium and potassium. A second possibility suggests itself. McCrudden (41) has shown that bone is constantly undergoing anabolism and catabolism. Is it possible that the calcium liberated in the process of catabolism is not available for anabolism but must be excreted? The negative calcium balance on a zero calcium intake might then be thought of as an index of the endo genous calcium metabolism. Experiments such as the ones now reported would thus be comparable to the early ones of Voit on nitrogen metabolism wherein the endogenous nitrogen metabolism was obtained by determining the nitrogen excretion during starvation (34) (39).

As a first step in the investigation of the cause of this negative calcium balance on a low calcium diet, it seemed of interest to see whether this relatively large amount of calcium ordinarily excreted on a very low calcium intake could be used during pregnancy to meet the fetal demands for calcium. Therefore, a young woman was put on a low calcium diet for three three-day periods during the fifth and eighth months of pregnancy and six weeks after delivery by Caesarian section. The findings are given in graphic form in figure 4. Some high calcium periods following the second and third group of low calcium intake periods are also charted, but will not be commented on here except to point out the rise in urinary calcium when the subject changed from a low calcium intake to a high calcium intake. It will be noted that this subject excreted practically the same amount of calcium in all three groups of low calcium periods, regardless of whether she was supplying a small amount of calcium to the fetus as in the fifth month of pregnancy, a large amount as in the eighth month of pregnancy, or none at all as during the second month after delivery, which was also one

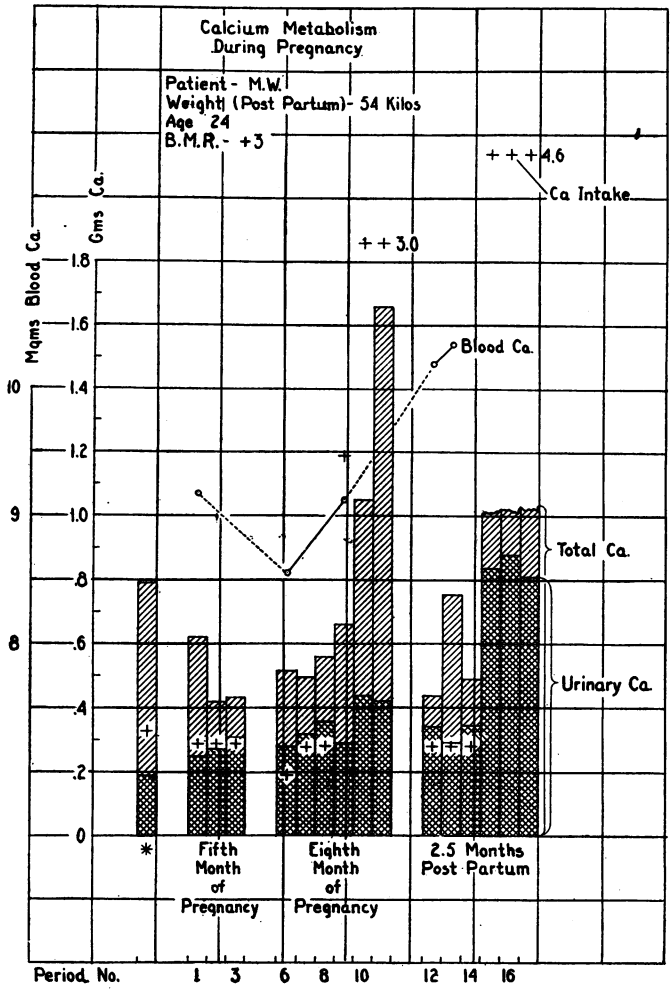

FIG. 4. CALCIUM METABOLISM DURING PREGNANCY

* Average calcium metabolism values of control series.

month after cessation of lactation. Furthermore, during all three periods of low calcium intake, this subject excreted about the same amount of calcium as she would have been expected to do had she not been pregnant, as judged from the average excretion of our normal controls. Attention is called to the fact that this subject's non-pregnant weight is 54 kgm. (average of controls 62 kgm.) and that her sex is opposite to that of the controls.

The serum calcium and phosphorus values of this patient are of interest. The serum calcium is confirmatory of the work of Widdows who found a low calcium level during pregnancy (35).

This experiment suggests that the calcium excreted on a low calcium diet is not available for the fetus, just as it is not available during growth for the building of bones (28).

SUMMARY

1. Figures showing the negative calcium balances in 46 three-day periods in thirteen normal individuals on a very low calcium intake are recorded.

2. It is pointed out that before the negative calcium balance of two normal individuals on a low calcium diet can be compared, factors should be introduced to equalize differences in sex, age, surface area, activity, acid-base properties of diet, values of other cations in diet, and phosphorus metabolism. It is further pointed out that unless two such individuals are in nitrogen equilibrium, further factors have to be introduced to offset the total acid value and the phosphoric acid content liberated during the destruction of the body protein.

3. Our results are compared with similar but not identical experiments from the literature.

4. It is emphasized that the negative calcium balance on a low calcium diet is an aspect of calcium metabolism which can be studied quantitatively under varying conditions.

5. The cause of the appreciable negative calcium balance on a low calcium diet is discussed.

6. Observations on a pregnant woman are included which tend to show that the calcium excreted on a low calcium diet is not available for the fetus. The calcium excretion during gestation is essentially normal.

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COMPOSITION OF THE DIETS EMPLOYED

Diet A

Substance	Weight	Protein	Fat	Carbo-hydrate	Calories	Ca	P
	grams	*grams*	*grams*	*grams*		*grams*	*grams*
Egg	100	13.4	10.5		148.0	0.067	0.180
Bread	30	2.8	0.4	15.8	77.7	0.008	0.028
Butter	10	0.1	8.5		76.9	0.002	0.002
Lettuce	30	0.4	0.1	0.9	5.7	0.013	0.013
Fresh tomato	50	0.5	0.2	2.0	11.5	0.006	0.013
Sugar	10			10.0	40.0		
Egg	20	2.7	2.1		29.6	0.013	0.036
Cream (18 per cent)	100	2.5	18.5	4.5	195.0	0.086	0.067
Total		22.4	40.3	33.2	584.4	0.195	0.339

Diet B

Substance	Weight	Protein	Fat	Carbo-hydrate	Calories	Ca	P
	grams	*grams*	*grams*	*grams*		*grams*	*grams*
Orange juice	100			10.8	43.0	0.029	0.016
Egg	50	6.7	5.3		74.0	0.033	0.090
Cream (40 per cent)	50	1.1	20.0	1.5	190.5	0.043	0.017
Sugar	10			10.0	40.0		
Apple	100	0.4	0.5	14.2	63.0	0.007	0.012
Egg white	30	3.7	0.1		15.3	0.005	0.004
Bread	50	4.7	0.6	26.4	129.5	0.014	0.047
Butter	10	0.1	8.5		76.9	0.001	0.001
Total		16.7	35.0	62.9	592.2	0.132	0.187

Diet C

Substance	Weight	Protein	Fat	Carbo-hydrate	Calories	Ca	P
	grams	*grams*	*grams*	*grams*		*grams*	*grams*
Egg	50	6.7	5.3		74.0	0.034	0.090
Egg yolk	100	15.7	33.3		363.0	0.137	0.567
Cream (18 per cent)	50	1.3	9.3	2.3	77.5	0.073	0.017
Sugar	10			10.0	40.0		
Apple	100	0.4	0.5	14.2	63.0	0.007	0.012
Egg white	30	3.7	0.1		15.3	0.005	0.004
Shredded Wheat	35	4.2	0.6	26.3	127.8	0.014	0.103
Milk	200	6.6	8.0	10.0	138.0	0.240	0.186
Sugar	10			10.0	80.0		
Total		38.6	57.1	72.8	958.6	0.480	0.939

Diet D

Substance	Weight	Protein	Fat	Carbo-hydrate	Calories	Ca	P
	grams	*grams*	*grams*	*grams*		*grams*	*grams*
Egg (whole)	170	25.8	17.9		251.6	0.1139	0.3060
Egg (white)	30	3.7	0.1		15.3	0.0045	0.0050
Egg (yolk)	100	15.7	33.3		363.0	0.1370	0.5240
Cream (18 per cent)	110	2.8	20.4	5.0	214.5	0.0946	0.0737
Sugar	30			30.0	120.0		
Apple	100	0.4	0.5	14.2	63.0	0.0070	0.0120
Milk	700	23.1	28.0	35.0	483.0	0.8400	0.6510
Shredded Wheat	35	4.2	0.6	26.3	127.8	0.0144	0.1134
Butter	50	0.5	42.5		384.5	0.0045	0.0085
Tenderloin	100	16.2	24.4		284.0	0.0093	0.1725
Lettuce	40	0.5	0.1	1.2	7.6	0.0172	0.0168
Asparagus	100	1.8	0.2	3.3	22.0	0.0250	0.0390
Bread	80	7.4	1.0	42.2	207.2	0.0216	0.0744
Celery	40	0.4		1.3	7.6	0.0312	0.0148
Cauliflower	100	1.8	0.5	4.7	31.0	0.1230	0.0610
Banana	100	1.3	0.6	22.0	99.0	0.0090	0.0310
Total		102.6	170.1	185.2	2,681.1	1.45	2.1023
Analyzed						0.994	1.756

Diet E

Substance	Weight	Protein	Fat	Carbo-hydrate	Calories	Ca	P
	grams	*grams*	*grams*	*grams*		*grams*	*grams*
Apple	330	1.3	1.7	46.9	207.9	0.0231	0.0396
Sugar	39			39.0	156.0		
Egg white	120	14.8	0.2		61.2	0.0180	0.0168
Cream (40 per cent)	195	4.3	78.0	5.9	743.0	0.1677	0.1307
Bread	195	18.7	2.7	99.6	498.3	0.0527	0.1814
Butter	75	0.8	63.8		576.8	0.0113	0.0128
Total		39.9	146.4	191.4	2,243.2	0.273	0.381
Analyzed						0.218	0.345