CALCIUM REQUIREMENT OF MAINTENANCE IN MAN.*

By H. C. SHERMAN.

With the Cooperation of A. R. Rose and M. S. Rose.

(*From the Department of Chemistry, Columbia University, New York.*)

(Received for publication, July 29, 1920.)

The demonstration upon laboratory animals by Osborne and Mendel,[1] that calcium necessarily occupies a prominent place in the inorganic food supply, and that of McCollum, Simmonds, and Parsons,[2] that calcium is one of the limiting factors in a very large proportion of our staple foods, lends added interest to the measurement of the calcium requirement in man and the comparison of the amount of calcium required for normal human nutrition with the amounts found in the ordinary freely chosen food of representative families or other groups of people.

Results obtained in this laboratory several years ago[3] indicated that, in so far as could be judged from the limited data determined at that time, it was by no means safe to assume that a freely chosen food supply would always furnish calcium in quantity sufficient to afford a safe margin above the actual requirements of normal nutrition.

Further study, therefore, seemed desirable and the purpose of the present paper is to summarize the data of a considerable number of additional laboratory experiments and to compare them with the findings of further observations upon actual food supplies.

* Published as Contribution No. 342 from the Department of Chemistry, Columbia University.

[1] Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, 1918, xxxiv, 131.

[2] McCollum, E. V., Simmonds, N., and Parsons, H. T., *J. Biol. Chem.*, 1919, xxxviii, 113, and in numerous other papers.

[3] Sherman, H. C., Mettler, A. J., and Sinclair, J. E., *U. S. Dept. Agric., Off. Exp. Stations, Bull. 227*, 1910.

In addition to the experimental data published from this laboratory in 1910,[3] 1918,[4] and 1919,[5] of which the latter have been recorded without as yet being discussed, studies upon the calcium requirement of maintenance have been made upon three healthy men, Subjects I, E, and R.

Subject I, weighing 61 kilos, consumed bread, milk, wheat breakfast food, egg whites, apple (or banana), rice, butter, and coffee, his daily calcium intake during each of six successive 4 day experiments being 0.46, 0.41, 0.41, 0.42, 0.32, 0.32 gm., respectively. The corresponding output in each of the six experiments was: in urine, 0.15, 0.18, 0.20, 0.20, 0.20, 0.20; in feces, 0.42, 0.50, 0.26, 0.34, 0.32, 0.21 gm. per day, respectively (Experiments 10 to 15 in Table I).

Subject E, weighing 69 kilos (Experiments 56 to 58 in Table I), after a preliminary period on calcium-poor food, took during a 3 day experiment a basal ration of bread, butter, and fruit with a calcium intake of 0.18 gm. per day; the daily output being 0.42 gm. (urine, 0.34, feces, 0.08 gm.). Without intermission there followed another 3 day experiment in which milk was added to the diet bringing the daily calcium intake to 0.39 gm., the output being the same (urine, 0.28, feces, 0.11 gm.), so that equilibrium was established at this figure. Then meat (lean beef) was added to the diet with the result that the daily calcium intake was increased by 0.01 gm. and the output rose 0.16 gm. (urine, 0.36, feces, 0.19 gm.). This loss of body calcium following the addition of meat to the diet might have been thought to be due to the fact that the added meat gave to the diet as a whole an excess of acid-forming over base-forming mineral elements; but other data obtained in this laboratory (Sherman, Gillett, and Pope[4]) do not indicate any such marked relation between the preponderance of acid- or base-forming elements in the food and the amount of calcium needed for maintenance.

[4] Sherman, H. C., Gillett, L. H., and Pope, H. M., *J. Biol. Chem.*, 1918, xxxiv, 373. Sherman, H. C., Wheeler, L., and Yates, A. B., *J. Biol. Chem.*, 1918, xxxiv, 383. Sherman, H. C., and Winters, J. C., *J. Biol. Chem.*, 1918, xxxv, 301.

[5] Sherman, H. C., Winters, J. C., and Phillips, V., *J. Biol. Chem.*, 1919, xxxix, 53.

TABLE I.*

Indicated Calcium Requirement for Maintenance per 70 Kilos of Body Weight per Day.

Experiment No.	Calcium.	Experiment No.	Calcium.	Experiment No.	Calcium.	Experiment No.	Calcium.
	gm.		*gm.*		*gm.*		*gm.*
1	0.29	25	0.64	49	0.39	73	0.50
2	0.28	26	0.44	50	0.61	74	0.60
3	0.82	27	0.56	51	0.43	75	0.50
4	0.42	28	0.70	52	0.58	76	0.41
5	0.35	29	0.54	53	0.53	77	0.37
6	0.66	30	0.53	54	0.53	78	0.42
7	0.46	31	0.39	55	0.58	79	0.40
8	0.66	32	0.49	56	0.30	80	0.40
9	0.61	33	0.55	57	0.29	81	0.39
10	0.65	34	0.48	58	0.40	82	0.42
11	0.78	35	0.35	59	0.28	83	0.39
12	0.54	36	0.28	60	0.28	84	0.33
13	0.61	37	0.30	61	0.27	85	0.45
14	0.61	38	0.27	62	0.29	86	0.33
15	0.49	39	0.32	63	0.30	87	0.50
16	0.40	40	0.34	64	0.60	88	0.37
17	0.42	41	0.29	65	0.55	89	0.54
18	0.44	42	0.46	66	0.59	90	0.40
19	0.33	43	0.42	67	0.54	91	0.31
20	0.41	44	0.41	68	0.55	92	0.44
21	0.35	45	0.43	69	0.47	93	0.35
22	0.40	46	0.46	70	0.46	94	0.29
23	0.40	47	0.50	71	0.40	95	0.33
24	0.53	48	0.47	72	0.55	96	0.38
						97	0.34
Average							0.45

* Experiments 1 and 2, Bertram, J., *Z. Biol.*, 1878, xiv, 354. No. 3, Renvall, G., *Skand. Arch. Physiol.*, 1904, xvi, 94. Nos. 4 and 5, von Wendt, G., *Skand. Arch. Physiol.*, 1905, xvii, 211. No. 6, Holsti, Ö., *Skand. Arch. Physiol.*, 1910, xxiii, 143. Nos. 7 to 9, Sherman, Mettler, and Sinclair.[3] Nos. 10 to 15, Rose, A. R., and Sherman, not previously published. Nos. 16 to 34, Sherman, Gillett, and Pope.[4] Nos. 35 to 48, Sherman, Wheeler, and Yates.[4] Nos. 49 to 55, Sherman, Gillett, and Pope.[4] Nos. 56 to 58, Sherman, not previously published. Nos. 59 to 63, Sherman and Osterberg, not previously published. Nos. 64 and 65, Sherman and Winters.[4] Nos. 66 to 75, Sherman, Winters, and Phillips.[5] Nos. 76 to 97, Rose, M. S., *J. Biol. Chem.*, 1920, xli, 349, and unpublished data.

Subject R, weighing 80 kilos, took during five consecutive 3 day experiments without intermission a diet of bread, butter, and apples furnishing an average daily intake for each of the five periods of 0.23, 0.21, 0.20, 0.21, 0.21 gm., respectively. The corresponding output for each experimental period was: in urine, 0.11, 0.17, 0.16, 0.18, 0.18; in feces, 0.21, 0.15, 0.15, 0.16, 0.16 gm. of calcium per day (Experiments 59 to 63 in Table I).

For purposes of comparison and discussion the data of all available experiments which seem to be quantitatively comparable (including, through the courtesy of Professor M. S. Rose, some unpublished experiments recently performed in her laboratory) have been computed to a uniform basis of daily calcium output per 70 kilos of body weight and the results brought together in Table I. Since calcium leaves the body so largely by way of the intestine, the error which may occur in the separation of the feces belonging to successive experimental periods is likely in the case of calcium to be more significant than in the case of phosphorus, and relatively much greater than in the case of nitrogen. Knowing by experience how readily a part of the calcium output properly belonging to an experimental period may thus be carried over into the one following, the writer has had this in mind in compiling the data of other investigators as well as those from his own laboratory and has sometimes treated two successive periods as one when convinced by examination of the protocols that a more trustworthy result is thus obtained. It will be seen that there are included in the table the data of 97 experiments (experimental periods of 3 to 8 days) showing an extreme range of 0.27 to 0.82 gm. and an average of 0.45 gm. per 70 kilos of body weight per day.

In the discussion of an analogous compilation of the data of experiments upon protein metabolism,[6] it was pointed out that in an appreciable proportion of those experiments the protein requirement was probably overestimated, largely because, influenced by previous overestimates of the amount of protein needed in nutrition, the experimenters did not reduce the protein intake to a low enough figure and for a long enough time really to determine the minimum amount on which equilibrium could have

[6] Sherman, H. C., *J. Biol. Chem.*, 1920, xli, 97.

been maintained. So far as this source of error is concerned the tendency in the study of calcium requirement has doubtless more often been in the other direction. In the past the calcium requirement of the body was underestimated. Experiments made to test calcium requirement have sometimes involved the use of diets furnishing so little calcium that the output (although greater than the intake) has been depressed below the point at which equilibrium could actually be maintained. Largely for this reason it is probable that some of the data for indicated calcium requirement in Table I, based as they are on the data of output when the intake was somewhat insufficient, are appreciably below the true requirements of the respective subjects. Doubtless there are other cases in which the requirement was overestimated through the use of diets unnecessarily rich in calcium for the purpose of the test; but these appear to be fewer in number and the general average of 0.45 gm. of calcium (equivalent to 0.63 gm. of CaO) is probably not above the true requirement.

Having now on record about 100 cases each of reasonably comparable experiments designed to measure the maintenance requirements for protein, phosphorus, and calcium, respectively, in normal human nutrition, it is of interest to compare the variability of the individual observations in the three series of experiments (each representing the work of several different investigators) and the probable errors of the three mean results as computed by accepted statistical methods.

The 109 experiments upon protein requirement[6] show a mean of 44.4 gm., a standard deviation of 9.07 gm., a coefficient of variation of 21, and a probable error of the mean of ±0.58 gm.

In 95 experiments upon phosphorus requirement[7] the mean with its probable error is 0.88 ± 0.01 gm., the standard deviation is 0.15 gm., and the coefficient of variation is 17.

The 97 experiments upon calcium requirement tabulated above give a mean result of 0.45 gm. with a probable error of ±0.008 gm. and show a standard deviation of 0.12 gm. and a coefficient of variation of 27.

In each of the three cases the data are now sufficiently numerous and consistent so that the probable error of the mean is

[7] Sherman, H. C., *J. Biol. Chem.*, 1920, xli, 173.

less than two one-hundredths of its value and therefore presumably as dependable as the accepted statements of average composition of even the most familiar of our staple foods.

It will be noted also that the coefficient of variation has been found to be of the same order of magnitude in the experimental study of protein, of phosphorus, and of calcium requirements. If any significance is to be attached to the slightly higher coefficient of variation in the data for calcium over those for protein or for phosphorus, it must follow that the case of calcium is the one which would seem to call for the most liberal margin of intake over the estimated average maintenance requirement if individual variability is to be covered by an ample factor of safety. Apparently a large proportion of American dietaries are open to improvement in this respect.

Comparing the present average of 0.45 gm. per man per day as the indicated calcium requirement with the previously reported average of 44 gm. as an indicated protein requirement, and keeping in mind the fact that the figure for protein is more likely to be an overestimate than that for calcium, and that the relative probable error due to individual variations is very similar in the two cases, we are forced to conclude that a food supply, in order to furnish these essential nutrients in relative proportions corresponding to the needs of the body, should contain at least 1.0 gm. of calcium (or 1.4 gm. of CaO) for every 100 gm. of protein. In the large majority of American food supplies of families and larger groups, as indicated by dietary studies made before the war by the United States Department of Agriculture and the New York Association for Improving the Condition of the Poor, this has not been the case. It does not follow that the calcium content was necessarily too low in the majority of dietaries, but rather that the food supply furnished a much more liberal surplus of protein than of calcium. When the results of 224 presumably typical American dietary studies were calculated to the usual basis of nutrients per man per day the average protein content was found to be 106 gm., or 140 per cent above the indicated maintenance requirement of 44 gm., while the average calcium content was 0.74 gm., or 64 per cent above the estimated actual minimum of 0.45 gm. Probably more significant than the average content of all the dietaries is the proportion of cases falling below the estimated requirement, either as regards protein, or as regards calcium. Only one of the 224 cases studied showed less protein than the indicated requirement, while one in every six was below the indicated requirement in calcium. In other words, the comparison of dietary studies or records of actual food supplies with the laboratory evidence of nutritive requirement suggests that very many more American dietaries are deficient in quantity of calcium than are deficient in quantity of protein, though of course there may be many cases in which the kind of protein, or the intake of some particular amino-acid, is unsatisfactory. If, in all the dietaries in the above group of 224 which showed less than 3,000 calories per man per day, the amount of food had been increased up to that level, there would have been no case of protein deficiency as judged by this standard while by the same criterion about 7 per cent or one in every fourteen of the dietaries studied would still be deficient in calcium. There seems to be no room for doubt that more attention should be given to the calcium intake both in human nutrition and that of farm animals. So far as the requirement for calcium in itself is concerned the intake may be supplemented by purely mineral additions as when the animal feeder includes finely ground rock phosphate ("floats"), bone ash, or oyster shells in the rations which he provides. Similarly calcium carbonate or phosphate might be habitually added to human food, either separately or by mixing it with the table salt used in seasoning; but it would probably be more difficult to persuade people generally to make such additions than to teach a more liberal use of foods naturally rich in calcium, while the latter course has the added advantage that the foods whose larger use would be invoked to increase the calcium intake (notably milk in its various forms) are important sources of proteins of high nutritive efficiency and of the fat-soluble vitamine as well.