Dear Editor,

In his Issues and Opinions article (1), Charles McCormick develops arguments why passive diffusion is not a functionally important route for calcium absorption in normal adults. He bases his arguments on an estimate of passive diffusion as reported in the article of Ireland and Fordtran who made measurements in the human jejunum (2). In that report, the slope of the function defined as “passive” is derived from and critically dependent on only two points that are quite close to one another. An estimate of a slope under these conditions is obviously hazardous. Ireland and Fordtran assumed the diffusible plasma calcium to be 1.5 mmol/L. A more correct value is 1.1–1.2 mmol/L (3). Using a value of 1.15 mmol/L for the intercept would almost double the slope of passive diffusion. If, in addition, the value for calcium secretion were only a little larger than that taken by Ireland and Fordtran, the rate of passive diffusion calculated from these two points would be even greater.

A more reliable method of estimating passive transport from the data of Ireland and Fordtran is to apply a straight line to the upper three values given in Figure 1 of their report (2), and then calculate the active and passive transport rates (4, 5). With this approach, active transport accounts for only ~27% of the total absorbed and assumes an absolute value close to what has been reported for the rat jejunum (6, 7). The calbindin content of the jejunum is much lower than that of the duodenum, and calcium is transported actively only in the proximal portion of the jejunum. Interestingly, this analysis [presented in full by Bronner et al. (5)] also yields a passive transport rate of 16%/h, a value previously established from a large number of experiments in rats.

Dr. McCormick also cites the work of Sheikh and colleagues (8) in support of his contention. Table 4 of that report indicates that when healthy young subjects increased their calcium intake from 502 to 1071 mg/d, their total absorption went up from 165 to 329 mg/d, with all of the increase due to the vitamin D-independent, i.e., passive, transport route. Thus, in this example from the human literature, passive absorption on a fairly typical calcium intake of 1 g constituted 79% of the total absorbed, clearly a major fraction.

We have shown (9) that in rats, the transit time of chyme through the duodenum is very short compared with the time spent in the ileum, where all calcium is absorbed by the passive route. There can be little doubt that the relative proportion of time spent in the duodenum and ileum in humans is not very different from that in lower mammals. When calcium intakes are low, it is the active calcium transport system, located largely in the duodenum, that comes into play. As calcium intake goes up, passive absorption dominates, in part because the active process, mediated largely by calbindin D₉k, is down-regulated in proportion to the increase in calcium intake (5, 7).

To be sure, the relative importance of active calcium transport is greater in human than rodent nutrition, essentially because rodents consuming laboratory rations consume more calcium per body weight than do humans. Nevertheless, the amount of calcium transported by the passive, diffusional route makes up a significant, often major fraction of the total absorbed in all species studied [e.g., Fig. 6 in Pansu et al. (10)]. Therefore, even though vitamin D administration does increase active calcium transport, increasing calcium intake is more effective and involves less risk for normal adults, notwithstanding the fact that this maneuver downregulates active calcium transport and causes a greater proportion of calcium to be absorbed passively.

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