

How important is dietary iron bioavailability?^{1,2}

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The high prevalence of iron deficiency in infants and in women of reproductive age and more recent concerns about iron overload in genetically susceptible persons emphasize the potential importance of dietary iron bioavailability. Meals with similar iron contents can differ severalfold in iron bioavailability when tested with use of a well-accepted test meal protocol. With this design, in the morning after an overnight fast, subjects consume single meals labeled with iron radiotracer and absorption is estimated by measuring isotope retention 2 wk later. Algorithms derived from these results facilitate the estimation of heme- and nonheme-iron absorption from diets, including the enhancing effect of ascorbic acid, meat, poultry, or fish and the inhibiting effect of phytate, polyphenols, calcium, egg, soy protein, or alcohol on nonheme-iron absorption (1).

Although ascorbic acid consistently enhances iron absorption from single meals in a dose-dependent manner and in a variety of dietary matrices (2), it has not been possible to longitudinally show increased body iron status with ascorbic acid supplementation of diets. This problem is not limited to ascorbic acid: in studies lasting several weeks or months, body iron status did not respond to controlled differences in ascorbic acid, calcium, phytic acid, or meat intake (citations in reference 3), all of which affect iron bioavailability in single-meal experiments. This dichotomy raises several questions: 1) Do single-meal results apply to practical diets? 2) Do single-meal results apply to whole diets under controlled conditions? 3) Does serum ferritin sensitively indicate longitudinal changes in iron absorption and bioavailability? 4) Does the body adapt to maintain iron homeostasis, thereby compensating for changes in iron bioavailability?

In this issue of the Journal, Cook and Reddy (4) address the first of these questions by comparing nonheme-iron absorption from a standard meal with that from three, 5-d subject-selected diets, 2 of which were high or low in ascorbic acid-containing foods (subjects selected or avoided these foods according to instructions from the investigators). The selection and implementation of the experimental diets by the subjects, which resulted in highly variable estimates of reported ascorbic acid intake, may largely account for the negative results of this study. In previous reports of iron absorption from a complete diet, the inhibiting effect of calcium on iron absorption was detectable when the diet was provided by the investigators (5) but not when the diets were selected and implemented by the subjects (6) as in the current report. Certainly, more pronounced results can be expected under more controlled dietary conditions. However, especially with single-meal tests, the investigator's enthusiasm may play a role; more extreme dietary differences can be imple-

mented than would be considered practical for long-term implementation by most people. The results of Cook and Reddy's (4) study indicate that counseling even highly compliant individuals to change their ascorbic acid intake will make little or no difference in iron absorption from complete diets.


The investigators noted that single-meal experiments may give more pronounced results with ascorbic acid because such experiments are conducted with subjects in a fasting state (4). However, iron absorption was not significantly different when identical meals were tested at breakfast after an overnight fast or at lunchtime, 4 h after a breakfast meal (7). Under controlled conditions, differences in iron absorption from complete diets can be as great as those from single meals (3, 8). Under similarly controlled test conditions, results of single-meal studies are consistent with studies of complete diets; the whole is not less than the sum of the parts.

The results from single-meal testing may overestimate the importance of dietary iron bioavailability, not only because of the limitations of practical diets, but also because of the relative insensitivity of serum ferritin to dietary change. Serum ferritin concentrations correlate well with body iron stores and are reduced by serial phlebotomy; this has resulted in guidelines that roughly equate differences of 1 µg ferritin/L in serum to 8–10 mg stored Fe (9). Although such guidelines suggest that small but detectable changes in serum ferritin will occur with differences in iron bioavailability over several weeks or months, such changes in serum ferritin have not been detected in longitudinal studies of dietary iron bioavailability. When longitudinal measures of serum ferritin and of iron absorption (from weighed, complete diets) were made in the same study, women's serum ferritin did not change significantly after 8 wk, despite substantial differences in absorbed iron (0.89 compared with 0.14 mg/d for an omnivorous compared with a vegetarian diet) (3). As discussed by Cook and Reddy (4), modest epidemiologic associations between serum ferritin and dietary factors (especially meat, rather than ascorbic acid) suggest that bioavailability does influence iron stores, but longitudinal changes occur more slowly and less substantially than predicted by the serum ferritin response to phlebotomy.

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Homeostatic control of iron stores by adaptation in iron absorption may provide at least a partial explanation for the disparity between the findings from single-meal studies and those from longitudinal measurements of iron status. Controlled complete diets that were intended to either maximize or minimize the iron bioavailability of Western diets differed 8-fold in total iron bioavailability when tested initially in adult men (8). This difference was reduced to 4-fold after 10 wk of dietary equilibration, independent of any change in serum ferritin (8). Although men's short-term adaptive control of iron absorption apparently is independent of serum ferritin (8), the inverse cross-sectional relation between serum ferritin and iron absorption (10) suggests that considerable additional absorptive adaptation would result from changes in body iron stores. Even short-term, adaptive responses may depend on body iron stores: women with low iron stores may be less likely than men to adapt their iron absorption to maintain the status quo.

We must not lose sight of the substantial effect of individual differences in iron status, which are controlled for and often corrected for when the iron bioavailability of meals or diets is evaluated. Whereas nonheme-iron absorption can vary by 2–5-fold because of dietary bioavailability, differences of 10–15-fold occur across a range of normal iron stores (3, 10). For heme iron, the control of absorptive efficiency suggested by both cross-sectional (10) and longitudinal (8) observations is considerably more modest. Consistent with the results of Cook and Reddy (4), individual iron status seems to be more influential than is bioavailability in determining nonheme-iron absorption, and iron status may be as influential as is bioavailability in determining total iron absorption from a complete diet. 

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