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Bioavailability of iron glycine

Dear Sir:

The title and conclusions of the article, "Bioavailability of iron glycine as a fortificant in infant foods," by Fox et al (1) are not supported by the data presented. Their data show that the absorption of iron from a glycine chelate is as well regulated by the body as is iron absorption from $FeSO_4$. Their data do not address bioavailability because regulation of iron absorption when there are sufficient iron stores in the body is the predominant feature of the research.

The first paragraph of the Results section states that the initial mean hemoglobin concentration of the subjects in study 1 was 114.0 ± 1.4 g/L and in study 2 was 118.0 ± 1.9 g/L. Rather than being iron deficient, the children involved in this test were iron sufficient from the beginning. Data from a 7-mo study involving 185 children with a broad range of iron status indicated that no significant change in hemoglobin status can be expected when initial hemoglobin concentrations are >110 g/L (2).

The claim of degradation of the chelate in the presence of phytates is hypothetical because no attempts were made to determine the molecular natures of the compounds being absorbed. The findings of other experiments indicate different conclusions. Isotope data of Bovell-Benjamin et al (unpublished observations, 1998) confirmed that iron glycinate does not mix with the inorganic iron pool, indicating that the iron glycinate must be absorbed differently than is $FeSO_4$. If the iron glycinate were being broken apart during digestion, there would be no differentiation of the iron pool.

In their discussion, Fox et al cited other investigations in support of their hypotheses. These citations are brief and do not represent all of the conclusions of the authors being cited. The researchers cited by Fox et al (3) actually stated that in their study of weanling rats, mean hemoglobin concentrations increased significantly ($P < 0.001$) with iron glycinate but not with $FeSO_4$. Liver concentrations were also higher with iron glycinate, but the increase was not significant because the animals were growing rapidly. The authors concluded, "Ferrous sulfate is often used as a standard with which to compare the bioavailability of different dietary sources of Fe, and it is unusual to find a compound that has Fe of higher bioavailability, but clearly, the Fe glycine complex was more readily utilized than ferrous sulfate" (3).

The fact that Fox et al included large amounts of ascorbic acid (0.83 mg ascorbic acid/mg Fe) with the $FeSO_4$ doses, but not with the iron glycinate chelate, suggests that they were actually intending to compare the absorption of ferrous ascorbate (and not $FeSO_4$) with that of iron glycinate. Fox et al cited the results of Olivares et al (4) as further proof of the lower bioavailability of the chelate than of $FeSO_4$. Olivares et al also claimed that the absorption of iron glycinate is no different from that of ferrous ascorbate. Olivares et al reported that $FeSO_4$ absorption in milk is only 4–5% compared with 15.4% (when normalized) for iron glycinate. They also reported that $FeSO_4$ absorption can double when ascorbic acid is added. Olivares et al concluded, "Iron bisglycine has a bioavailability comparable to that of $FeSO_4$, plus ascorbic acid in milk." When ascorbic acid was not present with $FeSO_4$, they found that iron glycinate had a bioavailability 2–2.5-fold higher than that of $FeSO_4$.

Finally, Fox et al conjecture that if their hypothesis that iron glycinate disassociates in a manner similar to that of $FeSO_4$ is correct, then iron glycinate will have the same poor organoleptic properties as $FeSO_4$. On the contrary, Olivares et al (4) state that iron glycinate (as the amino acid chelate) has low prooxidant properties and is stable when exposed to ambient air and temperatures. They further state that iron glycinate has a shelf life of >6 mo when mixed with milk and stored at room temperature.

In conclusion, it can be deduced from the data presented by Fox et al that absorption of iron from chelated iron glycinate is as well regulated by the body as is iron from $FeSO_4$ (or ferrous ascorbate) in situations in which there is not a great metabolic need for iron uptake, as indicated by a hemoglobin concentration >110 g/L. No data from a comparison of the bioavailability of iron glycinate and $FeSO_4$ (or ferrous ascorbate) are presented by Fox et al because sufficient iron stores existed at the onset of the study, ensuring that iron uptake from all sources would be tightly regulated by normal physiology to prevent the overabsorption of iron and its subsequent toxicity.

H DeWayne Ashmead

Albion Laboratories, Inc
101 North Main Street
Clearfield, UT 84015
E-mail: albionlabs@aol.com

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Reply to HD Ashmead

Dear Sir:

The results of our study entirely support Ashmead's proposal that absorption from iron glycine chelate is regulated to the same extent as that from $FeSO_4$ (or ferrous ascorbate). However, we disagree with his statement that we were not measuring bioavailability.

The conclusions drawn from our study are based on the measurement of hemoglobin incorporation of an oral dose of stable isotope–labeled $FeSO_4$ and stable isotope–labeled iron glycine chelate. This technique assumes that 90% of the absorbed iron is used for hemoglobin (1) and is a valid method for comparing the absorption and bioavailability of 2 different chemical forms of iron within the same individual (when 2 different stable isotopes are used to label the compounds). The use of subjects who are iron deficient would increase the sensitivity of iron absorption measurements. Although the infants in our study had hemoglobin concentrations >110 g/L, their neonatal iron stores would have been depleted by 9 mo of age and thus they would have had a high iron requirement due to rapid growth and, hence, a high efficiency of iron absorption. However, even in the absence of iron deficiency, the method used in our study would still be a valid technique to compare the bioavailability of different chemical forms of iron. As for Ashmead's comments on our earlier work, it is difficult to extrapolate iron absorption data from animal studies to humans because rats are known to have a higher fractional absorption of iron and are less sensitive to differences in iron bioavailability than are humans.

Many studies investigating the bioavailability or absorption of iron use a reference dose to normalize results between individuals. $FeSO_4$ in combination with ascorbic acid is the most commonly used reference dose and many researchers have used molar ratios of ascorbate to iron >1:1 [Cook et al (2), 2:1; Bezwoda et al (3), 10:1; and Hallberg et al (4), 10:1]. We used a molar ratio of 1:1 [iron as $Fe_2(SO_4)_3$] and most of the ascorbate involved in the reduction of ferric iron to ferrous iron would have been oxidized to dehydroascorbic acid or dioxogulonic acid. The resulting solution would therefore be mainly $FeSO_4$ and not ferrous ascorbate.

Our findings confirm that the iron glycine chelate is indeed a highly bioavailable form of iron because hemoglobin incorporation was comparable with that of freshly prepared $FeSO_4$ in the presence of ascorbic acid. Ashmead's comment that our reference to the work of Olivares et al (5) was further proof of the iron glycine chelate having a lower bioavailability is incorrect; we cited this reference in support of our observation that the absorption of iron glycine chelate and $FeSO_4$ are similarly affected by dietary modifiers. There was no mention made in our paper that the iron glycine chelate had a lower bioavailability than $FeSO_4$ or ferrous ascorbate. The absorption of iron from the glycine chelate was reduced by the presence of a known inhibitor of iron absorption, phytic acid. From this observation we concluded that some or all of the iron from the chelate had dissociated at some point and mixed with the intraluminal pool of ingested nonheme iron, where some of it was rendered unavailable through ligand formation with phytic acid.

Olivares et al (5), who used the same chelate we did (prepared by Albion Laboratories), also found that the absorption of iron glycine chelate was reduced by inhibitors found in milk and that a known enhancer (ascorbic acid) increased iron absorption from the chelate. These observations further substantiate our conclusion that iron is dissociated from the chelate in the gastrointestinal tract, where it can participate in chemical reactions with other dietary constituents. Exactly where, when, and how much of this dissociation takes place is open to further investigation. What can be postulated is that if the poor organoleptic properties associated with $FeSO_4$ under certain food conditions are not observed with the chelate, then dissociation of the iron glycine complex must be occurring within the gastrointestinal tract after ingestion. Ashmead cites unpublished work that apparently refutes our findings. Clearly, we cannot comment on this at present.

If absorption of the iron glycine chelate is being regulated by the body, as proposed by Ashmead in his letter, we must ask by what mechanism? If the iron chelate is absorbed intact by an amino acid transport mechanism, regulation would be governed by the presence of glycine and not iron. Thus, there would be no regulation of iron absorption per se. The other possibility is that the chelate dissociates and iron enters the common nonheme pool, the absorption of which is controlled by host-related factors such as iron stores, which is the mechanism indicated by our data and that of Olivares et al (5).

Thomas E Fox

Institute of Food Research
Norwich Research Park
Colney, Norwich NR4 7UA
United Kingdom
E-mail: tom.fox@bbsrc.ac.uk

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Mild cobalamin deficiency in older Dutch subjects

Dear Sir:

The report by van Asselt et al (1) is of great interest and I could not agree more with most of their conclusions. Permit me to add

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several of our observations in support and extension of theirs. We too have been impressed that half or more of the low cobalamin concentrations in the elderly (and others) cannot be explained by malabsorption (2–4). Because factors other than cobalamin status may affect serum cobalamin concentrations (4), it is important to keep in mind that 25% or more of the low cobalamin concentrations are not accompanied by any metabolic abnormalities and may not represent actual deficiency. Nevertheless, the causes responsible for the low concentrations, especially for the 75% that are associated with metabolic evidence of deficiency, need to be identified. Like van Asselt et al, we have found poor dietary intake of cobalamin to be virtually nonexistent in the elderly (5). Our data also support their observation of an ameliorative effect of cobalamin supplement use on cobalamin status, although it is noteworthy that many of our patients remained mildly deficient despite supplement use (5). Ironically, supplement use also appeared to be highest in subjects who had higher cobalamin intakes from food and, thus, presumably a lesser need for supplementation.

However, a strong word of caution is in order about any automatic equation between atrophic gastritis and food– cobalamin malabsorption. The 2 are not synonymous (3). Half of the patients with severe food– cobalamin malabsorption whom we biopsied and subjected to gastric analysis had neither atrophic gastritis nor achlorhydria (6). Thus, although nearly all patients with atrophic gastritis may have food– cobalamin malabsorption, many without atrophic gastritis may also have food– cobalamin malabsorption. Van Asselt et al might have found a higher prevalence of malabsorption and perhaps even a stronger association with Helicobacter pylori infection had they actually tested absorption directly.

It is too early in our still incomplete understanding of food-cobalamin malabsorption to allow ourselves the liberty of resorting to indirect markers when studying it. In recent years, various authors have proposed not only gastric and duodenal histology but serum gastrin concentrations, holotranscobalamin II concentrations, and other such substitutes for direct testing of food– cobalamin malabsorption. None of these substitutes were ever proven to be satisfactorily specific or sensitive, and at least one of the claims of equivalence has been retracted. I fear that unwarranted methodologic shortcuts will only add confusion to the subject.

As for Dr. Russell's accompanying editorial (7), early answers have begun to appear to his question concerning consequences of elevated methylmalonic acid concentrations (or more precisely, of mild, preclinical cobalamin deficiency). Over the years, we have consistently found electroencephalographic, evoked potential, and P300 potential abnormalities in half or more of our patients with metabolically defined, mild, preclinical cobalamin deficiency (8–10). In most cases, these abnormalities were reversed with cobalamin therapy. Moreover, mild but reversible clinical abnormalities, including neuropathy and memory loss were part of the picture in several patients. The extent of this subtle neurologic dysfunction and its contribution to the risks of mild cobalamin deficiency is an important area for further study.

Ralph Carmel

Department of Medicine
New York Methodist Hospital
50b Sixth Street
Brooklyn, NY 11215–9008
Email: rcarmel@pol.net

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Use of daily compared with weekly iron supplementation: apples and pears

Dear Sir:

About 10 y ago the World Health Organization (1) published recommendations on the design of large-scale iron supplementation programs with the aim of reducing the prevalence of iron deficiency anemia in populations of developing countries. One decade later, however, little has changed in the situation of iron deficiency anemia. Supplementation programs, when they exist at all, are largely ineffective for a variety of reasons, the most important being insufficient supply of iron tablets, low coverage of the target population, and poor compliance with tablet intake (2). A regimen that offers the possibility of lower cost, better compliance, and effectively raised hemoglobin concentrations in 2 or 3 mo is therefore surely worth consideration.

From the viewpoint of a clinician, Hallberg (3) appealed for the continued application in supplementation programs of the well-established, although inefficient, daily administration of iron and urged that supplementation on a weekly basis not be considered. His reason for this argument was that daily supplementation would provide a more rapid response in the treatment of anemia because the total amount of iron absorbed from a

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given dose would be ≈6 times larger from a dose divided into daily administrations than from a corresponding weekly dose.

Community-based studies in children and nonpregnant women from China (4), Bolivia (5), Indonesia (6–8), and Vietnam (9), however, did not show a marked difference in hemoglobin response to weekly or daily iron supplementation. The existence of mild-to-moderate rather than severe anemia, a long duration of supplementation, and high doses of iron were mentioned by Hallberg as reasons daily supplementation did not have a better effect on hemoglobin status than weekly supplementation in the these studies. First, the anemia prevalence of the studied populations was ≈20–50%, which is typical for populations in developing countries that are generally considered in need of supplementation (1). Although the prevalence was high, most subjects had mild-to-moderate forms of anemia. Nevertheless, a high prevalence of even mild degrees of anemia (hemoglobin: 90–110 g/L) has profound consequences for human development (1). Second, the duration and the dose of the daily iron supplementation were in line with recommendations for iron supplementation programs made by the World Health Organization (1). The duration of an intervention in a long-term prevention program should not be judged by comparison with a short-term therapeutic response, even though the studies also showed an adequate therapeutic response over the period of observation.

Hallberg also argued that hemoglobin concentrations would rise faster if high amounts of iron were given on a daily basis. This argument is valid and important for therapy in individuals with severe anemia in a hospital setting. However, speed of recovery has less importance in programs aimed at broad coverage, for which factors such as distribution, cost, and compliance are of high importance.

To date, only one study has been published on the effect of weekly supplementation in pregnant women (10). Hallberg laments the lack of a control group in this study and even doubts the ethical correctness of trials without a placebo group. This remarkable statement again uncovers conceptual differences between clinical theory and practical reality. The recommendation to include a placebo group may be relevant for clinical efficacy trials but is unethical in operational research in countries such as Indonesia where every pregnant woman is entitled to receive iron supplementation according to law. Hallberg also points to the low increase in hemoglobin concentrations in both the daily and weekly intervention groups (10). Although this is true, this study was carried out under program circumstances in which tablet intake was not supervised and under these conditions the effects of weekly and daily supplementation were not significantly different.

Innovation is required to solve the repeated problem of low effectiveness of daily iron supplementation programs under practical conditions. Studies published to date indicate that weekly supplementation may be a much cheaper option (11) for improving the iron status of children and nonpregnant women because it reduces anemia prevalence similarly to daily supplementation when used for the currently recommended duration. Because of the lack of completed studies, however, conclusive recommendations for pregnant women must await additional efficacy and effectiveness studies.

This is not the first and will not be the last discussion resulting from the misleading assumption that clinical experience with treatment can be uncritically applied to practical, population-based interventions. It is important to draw a clear line between appropriate therapy of moderate-to-severe anemia in individuals and cost-effective population-based programs. Let us recognize that apples are apples, and pears are pears. Both are valuable fruit and are tasty when eaten at the right moment of ripeness. But don't try to make an apple pie from pears!

Werner Schultink
Rainer Gross

Community Nutrition Program
University of Indonesia
GTZ/SEAMO
PO Box 3852
Jakarta 10038
Indonesia
E-mail: gtzseame@indo.net.id or gtzseam@ibm.net

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Reply to W Schultink and R Gross

Dear Sir:

It is obvious that Schultink and Gross misunderstood the essence

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of my critique of their recommendation to give iron weekly in combating iron deficiency (1). The concept that weekly administration of iron would be as effective as daily administration was based on the hypothesis that there is a mucosal block in the absorption of therapeutic doses of iron that makes a continuous (daily) supply of iron unnecessary, redundant, and irrational. As shown in my critical review (1), however, there is no such mucosal block during iron therapy in humans and thus no foundation for the concept of giving iron weekly. Actually, there is good quantitative evidence from 2 research groups that ≈6 times more iron is absorbed from daily doses than from weekly doses of the same total amount of iron (2, 3). At first glance it was then surprising that the therapeutic response—the increase in hemoglobin concentration—was almost the same after weekly compared with daily administration of iron in several studies. A reasonable explanation for these paradoxical findings, as pointed out in my analysis of these studies, is that the doses of iron given were high, the treatment periods were long, and the subjects included in the studies had only mild anemia. Because hemoglobin concentrations can reach only individual optimal concentrations, no valid comparisons of the efficacy of the 2 treatment models can be made; the therapeutic response can be expected to be the same under the conditions used. It would be expected, for example, that lower daily iron doses or much shorter treatment periods would result in the same increase in hemoglobin. Moreover, under such conditions even better compliance would be expected at a lower cost than that for administering high doses of iron weekly.

The arguments for weekly administration of iron used by Schultink and Gross are the "low effectiveness of daily iron supplementation programs under practical conditions" and that "innovation is required." It is certainly true that great efforts must be made to improve iron supplementation programs, especially in developing countries. For example, the delivery system of tablets must be improved so that tablets reach the target subjects; it is also desirable to improve the pharmaceutical properties of the iron tablets to increase their efficacy and reduce side effects. It is time to take new initiatives in this area (4). A further important area for research, initiated for example by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF), would be the development of better methods to motivate subjects to take tablets, for example, during pregnancy. I certainly share the disappointment of Schultink and Gross that so little has been done to combat iron deficiency by the WHO, UNICEF, and the countries involved. It is important to emphasize, however, that a change to the less-efficient weekly administration of iron would not solve the key problems of good efficacy, adequate tablet distribution, and high motivation.

Schultink and Gross do not seem to understand that before starting national or regional supplementation programs or any diagnostic, prophylactic, or therapeutic program, it is important to critically examine the effectiveness of such programs, including costs. This is not just a clinical approach that is "uncritically applied to practical, population-based interventions." The use of carefully controlled studies, with inclusion of groups given placebo, is a standard not only in clinical trials but also in field studies in developing countries. This fundamental approach has been discussed in detail in different publications from the WHO over the years on the basis of work of experts from countries where iron deficiency anemia is both common and severe and is not based solely on the work of so-called "clinicians." In all these reports and recommendations it is clearly stated that subjects should first be divided into groups according to severity of anemia (because the therapeutic response is related to the severity of anemia) and then be randomly allocated to different groups that will be given, for example, different doses of iron. It is also clearly emphasized that one of the groups must be a placebo group so that both effects and side effects can be evaluated (5–7). For ethical reasons, those with more severe iron deficiency anemia are excluded. The cutoff for severe iron deficiency anemia is different in different countries. In some of the Indian studies (8) and in the WHO reports (5, 6) the limit was set at a hemoglobin concentration of 80 g/L. In other studies cutoffs as high as ≤120 g/L were used (9). The details of the experimental design may also vary in different studies, for example, if the role of folate deficiency is also tested or if the effects of hookworm infestation are excluded.

The statement that controlled studies of pregnant women are not allowed in Indonesia is surprising. Even so, controlled studies can be carried out in any of the many other countries where daily and weekly administration of iron have been compared. The strict attitude of the ethics committees in Indonesia toward assignment of pregnant women to placebo groups makes it hard to believe that iron supplementation with a dose associated with one-sixth of the absorption of daily doses could ever have been approved.

The development of good iron supplementation programs is important considering our increasing awareness of the importance of an optimal supply of iron in infants, children, and adolescents. It is important that future work in developing countries be based on adequate, carefully controlled studies. The metaphor that such studies are apples and the ones carried out by Schultink and Gross are pears does not necessarily form a good basis for a fruitful discussion of an important topic.

Leif Hallberg

Institute of Internal Medicine
Department of Clinical Nutrition
Sahlgrenska University Hospital
University of Göteborg
Annedalsklinikerna
S-41345 Göteborg
Sweden

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No evidence for dietary protein and dietary salt as main factors of calcium excretion in healthy children and adolescents

Dear Sir:

Itoh et al (1) state new evidence in their recent paper in this Journal that protein intake is a main factor of calcium excretion. They report detailed findings on the relation between protein, sodium, and calcium intakes and calcium excretion. Moreover, they provide estimates of the size of the effect. In what follows, I will explain some weaknesses in their data interpretation that may have resulted in overestimation of the effects. In addition, I have evidence of a different finding in healthy children and adolescents, and hence conclude that in these populations there is no evidence that dietary salt and dietary protein are main factors of calcium excretion.

Itoh et al state that errors in the measurement of daily dietary protein intake are relatively high. It is well known that measurement error in factor variables causes biased effect estimates in standard multiple regression and that the bias depends on the accuracy of the measurement—see review by Reeves et al (2). Therefore, the authors used urinary urea excretion and urinary sulfate excretion to assess the effect of the components of protein intake. Urinary measurements of urea, sulfate, calcium, and sodium in Itoh et al's study were likely to have correlated measurement errors because the measurements were made in the same urine sample. Consequently, a crucial assumption of standard multiple regression analysis was not valid. The inappropriate use of multiple regression analysis led to the unjustified conclusion that dietary salt and protein intakes have a major effect on calcium excretion. Two other studies also report evidence that dietary salt is a main factor regulating calcium excretion; however, both of these studies suffer from the same misuse of multiple regression and consequently their findings are not valid (3, 4).

In a preliminary interim analysis of data from the Dortmund Longitudinal Study (5) in healthy German children and adolescents aged 2.8–18.3 y (1985–1997: n = 187 boys and 850 observations and n = 180 girls and 807 observations), Lausen (6) showed that interindividual variation, reciprocal relative growth velocity [(Δcm/y)/cm], and dietary protein intake (g/d) are the most important factors regulating urinary calcium excretion (mg/d). Other significant factors are magnesium intake (mg/d), sodium intake (mg/d), calcium intake (mg/d), and phosphorus intake (mg/d). The longitudinal data show that individual excretion explained 69% of the variance in the data ($R^2 = 0.69$).

In summary, evidence for dietary protein and dietary salt as main factors of calcium excretion when intakes of protein, salt, and calcium are within usual ranges is not convincing.

Berthold Lausen

Department of Medical Statistics and Evaluation
Imperial College of Science, Technology and Medicine
Du Cane Road
London W12 0NN
United Kingdom
E-mail: b.lausen@rpms.ac.uk

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Reply to B Lausen

Dear Sir:

We appreciate greatly the sound criticism of Lausen on the weakness of the data interpretation in our study. Recently, we also realized the bias in the analysis of the relation of the measured variables in the same 24-h urine specimens. As Lausen correctly pointed out, the positive correlations observed among the measurements of daily calcium excretion were possibly due to errors commonly associated with urinary specimens, especially errors that occur in 24-h urine collections, although we carefully excluded subjects who appeared to have had problems with urine collection. Thus, we reanalyzed the data from our previous study using daily excretions of various urinary constituents corrected for daily urinary creatinine excretion (1). The results of multiple regression analyses still showed significant and positive correlations between calcium-creatinine, urea-creatinine, calcium-creatinine, and sodium-creatinine ratios after adjustment for sex, age, and calcium intake in both age groups: 20–49- and 50–79-y-olds.

Of course, we recognize that multiple regression analysis does not completely eradicate the bias. However, multiple regression analyses showed that the daily dietary intake of protein estimated from dietary records was significantly and positively correlated with daily calcium excretion in the same population (1).

The reciprocal association between urinary calcium excretion and dietary protein intake observed by Lausen in healthy children and adolescents is an interesting and important finding. The association is reasonable because protein is an important constituent of bone, and young individuals, contrary to adults, require large amounts of protein for bone growth and are in strong positive

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nitrogen balance. It is highly possible that low protein intakes prevent effective utilization of dietary calcium for bone formation, resulting in an increase in urinary calcium excretion.

Roichi Itoh

Department of Home Economics
Tokyo Kasei Gakuin University
2600 Aiharamachi, Machida-City
Tokyo 194–0292
Japan
E-mail: ysuyama@tka.att.ne.jp

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Erratum

Mendoza C, Viteri FE, Lönnerdal B, Young KA, Raboy V, Brown KH. Effect of genetically modified, low–phytic acid maize on absorption of iron from tortillas. Am J Clin Nutr 1998;68:1123–7.

Table 4 was inadvertently omitted from the article during production.

TABLE 4
Iron absorption from study diets and ferrous ascorbate[1]

	100% WTM tortillas	50% WTM + 50% LPM tortillas	100% LPM tortillas	Reference dose
Iron absorbtion (% of dose)	1.93 (1.27, 2.97)[a]	1.65 (1.13, 2.40)[a]	2.88 (1.93, 4.29)[b]	14.14 (10.88, 18.40)
Relative iron absorbtion (%)[2]	5.48 (4.56, 9.26)[a]	4.66 (3.22, 6.23)[a]	8.15 (5.48, 11.33)[b]	—

[1] Geometric $\bar{x}$; 95% CI in parentheses. n = 13. WTM, wild-type maize; LPM, low–phytic acid maize. Means within a row with different superscript letters are significantly different, $P < 0.05$ (repeated-measures ANOVA on unadjusted values and on the relative values followed by post hoc Tukey's analysis).

[2] Percentage after adjustment to 40% of reference dose absorption.

Erratum

Åkesson A, Bjellerup P, Berglund M, Bremme K, Vahter M. Serum transferrin receptor: a specific marker of iron deficiency in pregnancy. Am J Clin Nutr 1998;68:1241–6.

Parentheses were inadvertently omitted from the equations used to calculate sensitivity, specificity, positive predictive value, and negative predictive value. On page 1242, the first paragraph of the "Statistical analyses" section should read as follows:

> Sensitivity was defined as $TP/(TP + FN) \times 100$ and specificity as $TN/(TN + FP) \times 100$, where TP is true positive, FN is false negative, TN is true negative, and FP is false positive. Positive predictive value was defined as $TP/(TP + FP) \times 100$ and negative predictive value as $TN/(TN + FN) \times 100$.

Erratum

Dreon DM, Fernstrom HA, Campos H, Blanche P, Williams PT, Krauss RM. Change in dietary saturated fat intake is correlated with change in mass of large low-density-lipoprotein particles in men. Am J Clin Nutr 1998;67:828–36.

In Table 2, on page 832, all lipoprotein mass values should be given as mg/L as follows:

TABLE 2
Plasma lipoprotein concentrations in all subjects[1]

	Low-fat diet	High-fat diet
Lipoprotein mass (mg/L)		
VLDL	1273.0 ± 88.4	759.1 ± 61.0[2]
IDL	334.9 ± 16.6	328.6 ± 16.4
LDL		
LDL-I (S_f^0 7–12)	924.4 ± 39.1	1318.3 ± 45.6[2]
LDL-II (S_f^0 5–7)	1067.0 ± 34.8	1225.7 ± 38.1[2]
LDL-III (S_f^0 3–5)	812.6 ± 39.8	598.2 ± 37.6[2]
LDL-IV (S_f^0 0–3)	179.9 ± 15.2	109.5 ± 10.2[2]
HDL_2	246.4 ± 24.1	369.4 ± 33.9[2]
HDL_3	1819.8 ± 30.6	1907.3 ± 32.6[3]

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