Association between plasma zinc concentration and zinc kinetic parameters in premenopausal women


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Yokoi, Katsuhiko, Norman G. Egger, V. M. Sadagopa Ramanujam, Nancy W. Alcock, Hari H. Dayal, James G. Penland, and Harold H. Sandstead. Association between plasma zinc concentration and zinc kinetic parameters in premenopausal women. Am J Physiol Endocrinol Metab 285: E1010–E1020, 2003 First published July 15, 2003; 10.1152/ajpendo.00533.2002.—The objective of this study was to measure relationships between plasma zinc (Zn) concentrations and Zn kinetic parameters to measure relationships of Zn status with taste acuity, food frequency, and hair Zn in humans. The subjects were 33 premenopausal women not taking oral contraceptives and dietary supplements containing iron and Zn. Main outcomes were plasma Zn concentrations, Zn kinetic parameters based on the three-compartment mammillary model using 65Zn as a tracer, electrical taste detection thresholds, and food frequencies. Lower plasma Zn was significantly (P < 0.01) associated with smaller sizes of the central and the lesser peripheral Zn pools, faster disappearance of tracer from plasma, and higher transfer rate constants from the lesser peripheral pool to the central pool and from the central pool to the greater peripheral pool. The break points in the plasma Zn-Zn kinetics relationship were found between 9.94 and 11.5 μmol/l plasma Zn. Small size of the lesser peripheral pool was associated with lower frequency of beef consumption and higher frequency of bran breakfast cereal consumption. Hypopitocinemic women with plasma Zn <10.7 μmol/l or 700 ng/ml had decreased thresholds of electrical stimulation for gustatory nerves. Our results based on Zn kinetics support the conventional cutoff value of plasma Zn (10.7 μmol/l or 700 ng/ml) between normal and low Zn status.

HUMAN ZINC (Zn) deficiency occurs worldwide (9, 19, 47, 48). The National Health and Nutrition Examination Survey 2 (NHANES-II) found that many women choose diets low in iron (Fe) and Zn and that the 25th percentile for serum ferritin of premenopausal women was 14 μg/l, a level consistent with absent bone marrow Fe (22). NHANES-III found that the 10th percentiles of Zn intake for women from 19 to 30 yr old were 6.33 mg, which is similar to the estimated average requirement (6.8 mg) of Zn for this age group of women (15). Therefore, a certain portion of the female population might be low in Fe and/or Zn nutriture. Consistently, low serum ferritin concentrations (low Fe status) and low Zn status tend to be associated in the United States (49, 70). However, the prevalence of Zn deficiency in the United States is not known, because diagnostic criteria of low-Zn status are not still established.

Plasma Zn concentration is a popular Zn index in the clinical field. As a criterion of low Zn status, 10.7 μmol/l (700 ng/ml) of plasma (or serum) Zn, a value approximately two SD below the adult mean, has been used (18). Kinetic indexes of Zn can be a versatile tool to evaluate Zn status more precisely than plasma Zn (46). The presence of a break point between the plasma Zn-Zn kinetic parameter relationship provides evidence for the cutoff value between normal and abnormal Zn nutriture.

Several researchers used Zn kinetic parameters to precisely evaluate Zn metabolism and nutriture. Prasad et al. (44) found the rapid disappearance of 65Zn tracer from plasma in the stunted boys with hepatosplenicomegaly and hypogonadism that were later corrected by supplemental Zn. Rapid disappearance of stable Zn tracer from plasma was also found in premenopausal women with low Fe store (70) and men receiving experimental diets low in Zn (29, 30). Miller et al. (38) found a positive correlation between Zn intake and rapidly exchangeable Zn pools that completely turned over within ~48 h.

To use Zn kinetic parameters in a larger clinical investigation for a general population, there are two technical problems to be solved. The first problem is the precision in Zn tracer analyses. Radioactive Zn isotopes were first used as tracers (1, 2, 16, 44, 46, 60) but replaced by stable Zn isotopes later (11, 29, 30, 34, 38, 41, 43, 53, 58, 60, 61, 68–70) to avoid radiation exposure. However, imprecision of stable isotope analyses by inductively coupled plasma-mass spectrometry for...
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Routine use can be substantial. This fact prompted us to quantitatively evaluate effects of measurement errors in stable isotope analyses on the model fitting.

The second problem is the length of observation periods after administration of tracers. Wastney et al. (63, 64) emphasized in their comprehensive review that the existing Zn kinetic models (43) usually require extensive sample collection for a week or longer. These models can provide precise kinetic parameters, although they impose practical difficulties for larger clinical investigations. There is a need to explore methods for obtaining Zn kinetic parameters consistent to other existing models using shorter observation periods. Therefore, we examined a closed mammillary model with three compartments over a 24-h observation period after an intravenous dose of Zn tracer.

Our aim was to determine the relationship between plasma Zn concentration and Zn kinetic parameters and find the critical cut-off value for plasma Zn that would distinguish between adequate and inadequate Zn nutrition based on this relationship. In addition, we determined relationships between plasma Zn and food frequencies and taste acuity.

SUBJECTS AND METHODS

Design. This report describes baseline findings from a treatment trial of Zn and/or Fe supplements on cognition of premenopausal women. The results of treatment will be reported elsewhere. This study was approved by the Institutional Review Board of the University of Texas Medical Branch (UTMB), and written consents were obtained from all participants of the study.

Subjects. The participants were 33 premenopausal women selected from 708 individuals living in Texas of various ethnic backgrounds who expressed potential interest through their telephone response to advertisements. The selection was extended to UTMB for screening.

From the 708 individuals who expressed potential interest, 323 respondents were interested at participating in the study. From these 323 respondents, 129 subjects met the selection criteria. Zn kinetics were measured in the first 50 subjects of these 129 evaluated subjects after the subjects had taken a supplement of micronutrients that did not include Zn or Fe for at least 7 days. The purpose of the micronutrient supplementation was to prevent unappreciated deficiencies from affecting the study. Micronutrients were designed based on the 1989 Recommended Daily Allowance. The composition of micronutrients was reported previously (50). Finally, 33 of these 50 subjects were not taking oral contraceptives and were selected for further analyses in this report.

Outcomes. The main baseline outcomes relevant to this report were food frequency, taste thresholds, and indexes of Fe and Zn status. Of the latter, Zn kinetics were measured on day 8–12 of the menstrual cycle.

Zn kinetics. The procedures for Zn kinetics were reported previously (69, 70). Subjects were admitted to the General Clinical Research Center. Meals provided <6 mg Zn/24 h. The first night, subjects were fasted for at least 8 h. The next morning, soon after awakening, a 24-h urine collection was started. Urine was collected using a plastic “hat” and plastic bags were processed with 1% nitric acid and deionized water. Subsequently, aliquots were stored at −20°C.

Blood samples were collected, using trace metal-free syringes and tubes, for indexes of Fe and Zn status. A hair sample was collected from the occipital scalp and placed in a disposable Falcon polypropylene test tube for storage. For administration to the subjects 67Zn chloride was prepared from 67Zn oxide (67Zn natural abundance, 4.11%; enrichment, 93.11%; Oak Ridge National Laboratories, Oak Ridge, TN), as reported previously (69). The 67Zn chloride solutions were tested for sterility (Dept. of Clinical Microbiology and Immunology, UTMB) and pyrogenicity (Scientific Associates, St. Louis, MO).

Short Tedilon catheters were placed in both antecubital veins of the subject. The catheters were attached to a drip of normal saline by a three-way stopcock. A baseline blood sample was taken. Next, 2 mg 67Zn dissolved in normal saline was administered over 3 min through the stopcock. This was followed by rapid administration of saline for 1 min. Samples of at least 10 ml were taken from the other arm at 5, 15, 30, 45, 50, 60, and 90 min and 2, 6, 12, and 24 h after administration of 67Zn. Before each collection, 2 ml blood was drawn to remove saline and diluted blood from the catheter. The blood samples were collected into a “Monovette” syringe (Sarstedt, Germany) containing lithium heparin (10 U/ml blood). After collection, the samples were placed in ice until delivery to the laboratory.

Body composition measurement. The next day, body composition was assessed while fasting. Height (nearest cm) and weight (nearest 0.1 kg) were measured. Next, lean body mass was determined by bioelectrical impedance analysis (BIA) using a BIA 101A analyzer (RIJ Systems, Clinton, MI) that provided a current of 800 μA at 50 kHz. Lean body mass (nearest 0.1 kg) was calculated using the software (Weight Manager version 2.05a) provided by the manufacturer.

Chemical analyses. Chemical analysis was done on batches of samples. To remove contaminants, hair samples were washed with acetone, threefold with purified water (MilliQ; Millipore, Bedford, MA), and again with acetone (27). The hair, plasma, and urine samples were digested with hydrochloric acid (3) and dissolved in 1% nitric acid. Plasma and hair Zn were analyzed by flame atomic absorption spectrometry (3). 67Zn-to-65Zn ratios in plasma were measured by using an inductively coupled plasma-mass spectrometer VG PlasmaQuad-1, upgraded to a PlasmaQuad-2 plus status (VG Instruments, Winsford, UK; see Ref. 45). The coefficient of
variation of the isotope ratio measurement was 0.2–0.6%. Each sample was analyzed with 10 replicate runs to obtain optimal precision (see the supplementary material, available at the American Journal of Physiology: Endocrinology and Metabolism web site).

Calculation of Zn kinetic data. The tracer-to-tracer ratio (TTR) was calculated based on the approach of Cobelli et al. (10)

\[
TTR = \left(\frac{A_{667} \times IR - A_{667}}{A_{667} - A_{668} \times IR}\right)
\]

where IR is the isotope ratio of \(^{67}\)Zn to \(^{68}\)Zn, \(A_{667}\) is the natural abundance of \(^{67}\)Zn, \(A_{668}\) is the natural abundance of \(^{68}\)Zn, and \(A_{667}\) is the abundance of \(^{67}\)Zn in the enriched preparation, and \(A_{668}\) is the abundance of \(^{68}\)Zn in the enriched preparation.

The disappearance of Zn tracer from plasma was described by a four-exponential function (38, 44)

\[
TTR = H_0 e^{-\gamma_3 t} + H_1 e^{-\gamma_2 t} + H_2 e^{-\gamma_1 t} + H_3 e^{-\alpha t}
\]

where \(g_1 > g_2 > g_3 > g_4\), H’s refer to the coefficients for each term and \(g_1-g_4\) are the coefficients for each exponential.

If \(g_1 \gg g_2 \gg g_3 \gg g_4\) as is generally found in Zn kinetics (38), the truncated form of the polynegative function (the biexponential function with a constant term) can be substituted for the complete form when the observation period is shorter than the half-life of the third term, ~6 days (see the supplementary material, available at the American Journal of Physiology: Endocrinology and Metabolism web site)

\[
TTR = H_0 e^{-\gamma_3 t} + H_1 e^{-\gamma_2 t} + H_2 e^{-\alpha t}
\]

There are two possible three-compartment models corresponding to the above function, i.e., closed mammillary model and closed catenary model. We selected the closed mammillary model so as to accommodate the simpler biological interpretation (Fig. 1). In a mammillary model, all peripheral compartments are directly connected to the central compartment without any direct connections between peripheral compartments (33). The model consists of compartments, transfer rate constants, \(k_{ij}\), which represent fractional transfer into compartment \(i\) from compartment \(j\) per unit of time, and fluxes, \(F_{ij}\), which represent the mass of Zn transferred into compartment \(i\) from compartment \(j\) per unit of time. A subscript “o” denotes the outside of the system. The transfer rate constants \(k_{ii}\) represent the sum of the outward transfer rate constants of compartment \(i\).

For an open (almost closed) model, \(k_{02} = 0\) and \(k_{03} = 0\). Subsequently, \(Q_2\) and \(Q_3\), and the transfer rate constants \(k_{ij}\) are uniquely determined. From the coefficients in the triexponential function, the kinetic parameters in the mammillary model were calculated according to Landaw et al. (33)

\[
k_{11} = k_{01} + k_{21} + k_{31} = \sum_{i=1}^{3} H_i g_i
\]

Roots of the numerator of the Laplace transformation of the triexponential function, i.e., the solutions of the following quadratic equation with the unknown variable, \(s\), give \(k_{22} (=k_{12} + k_{02})\) and \(k_{33} (=k_{13} + k_{03})\) according to Landaw et al. (33)

\[
s^2 \sum_{i} H_i + s \sum_{i} H_i g_i + \sum_{i} H_i g_i g_i = 0
\]

\[
\gamma_2 \text{ and } \gamma_3 \text{ are then calculated as follows}
\]

\[
\gamma_j = k_{ij} k_{ji} = \frac{\sum_{i=1}^{3} H_i}{\sum_{i=1}^{3} (k_{ij} - g_i)^2}
\]

The following analytical solutions are then derived

\[
Q_1 = \frac{D_0}{H_1 + H_2 + H_3}
\]

\[
Q_2 = \frac{k_{21}}{k_{12}} Q_1
\]

\[
Q_3 = \frac{k_{31}}{k_{13}} Q_1
\]

\[
EZP = Q_1 + Q_2 + Q_3
\]

\[
F_{12} = F_{21} = k_{12} F_{22}
\]

\[
F_{13} = F_{31} = k_{13} F_{33}
\]

\[
TR = F_{21} + F_{31} = k_{11} Q_1
\]

where \(Q_1\) is the plasma Zn (central) compartment, \(Q_2\) is the lesser peripheral Zn compartment, \(Q_3\) is the greater peripheral Zn compartment, \(D_0\) is the dose of tracer administered, \(EZP\) is the rapidly exchangeable Zn pool, and TR is the plasma Zn turnover rate.

For the closed mammillary model that corresponds to the truncated triexponential model, \(k_{01}\) is equal to 0. When the
coefficients in the polyexponential function are given, all parameters in the mammillary model can be solved. Independent from the tracer kinetics, the urinary Zn excretion rate (UZnExR) was determined by using total Zn in the 24-h urine sample. The urinary Zn excretion rate constant was calculated based on the assumption that excreted Zn originated from plasma (60, 62). Subsequently, urinary Zn excretion rate constant was calculated as UZnExR divided by Q2.

Computations and statistics were done using SYSTAT 5 for Macintosh version 5.2.1 software (SYSTAT, Evanston, IL) and Prism version 2.0 for Macintosh (GraphPad Software, San Diego, CA). TTR disappearance data were logarithmically transformed to give appropriate weight to data assumed to have proportional variance for the subsequent regression analysis (8). Logarithmically transformed TTR was fit to the truncated triexponential function by the nonlinear regression procedure using the simplex method in the software. The kinetic parameters in the closed mammillary model were calculated from the coefficients in the truncated triexponential function with Microsoft Excel.

**RESULTS**

Relationship between plasma Zn and Zn kinetic parameters. Table 1 shows the characteristics of the 33 subjects. The subjects were premenopausal women composed of 21 whites, 4 blacks, 1 Asian, and 7 women who had Hispanic surnames. Because apparent Fe deficiency anemia was excluded at the screening, the Hb level was >110 g/l. The number of subjects with serum ferritin concentration <20 μg/l was 21. The number of subjects with Fe-deficient erythropoiesis (erythrocyte protoporphyrin >1,000 μg/l) was three. All subjects with Fe-deficient erythropoiesis had serum ferritin <20 μg/l. Seventeen subjects had plasma Zn concentrations <10.7 μmol/l (700 ng/ml).

Table 2 shows the Zn kinetic parameters of these subjects. Figure 2 shows the typical fit of the model to TTR data in plasma obtained from subject 18. The median R2 was 0.9990, with a range of 0.9930–0.9998. The averages of asymptotic SEs were 0.10, 13, 0.007, 2.2, and 0.0009, respectively, for H1, R1, H2, R2, and H3. The variation of the Zn pool size Q2 was larger than Q1 and Q3. Plasma Zn positively correlated with Q1, Q2, and F21. Body weight positively correlated with Q1, EZP, F31, and TR. Because lean body mass significantly or marginally correlated with Q1, Q3, EZP, F31, and TR (Table 3), those parameters were divided by lean body mass, and the quotients were used for the further statistical analyses. A variation in Q1, Q2, Q3, EZP, F21, F31, and TR per lean body mass was smaller than in those without correction by lean body mass (Table 2).

Plots of Plasma Zn and Zn kinetic parameters suggested nonlinearity between plasma Zn and g1, g2, k11, k22, and TR (Table 3), those parameters were divided by lean body mass, and the quotients were used for the further statistical analyses. A variation in Q1, Q2, Q3, EZP, F21, F31, and TR per lean body mass was smaller than in those without correction by lean body mass (Table 2).

Table 1. Characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>30.2 ± 5.2</td>
<td>30.0</td>
<td>19.0</td>
<td>39.0</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>64.8 ± 14.4</td>
<td>60.0</td>
<td>45.8</td>
<td>108.4</td>
</tr>
<tr>
<td>Body height, m</td>
<td>1.62 ± 0.07</td>
<td>1.61</td>
<td>1.49</td>
<td>1.78</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24.7 ± 5.5</td>
<td>22.7</td>
<td>18.1</td>
<td>38.4</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>45.0 ± 6.4</td>
<td>43.6</td>
<td>34.0</td>
<td>65.2</td>
</tr>
<tr>
<td>Plasma zinc, μmol/l</td>
<td>10.7 ± 1.6</td>
<td>10.5</td>
<td>7.5</td>
<td>14.4</td>
</tr>
<tr>
<td>Serum ferritin, μg/l</td>
<td>23.2 ± 16.9</td>
<td>18.0</td>
<td>6.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Serum iron, μmol/l</td>
<td>12.8 ± 6.7</td>
<td>11.4</td>
<td>5.1</td>
<td>32.2</td>
</tr>
<tr>
<td>Erythrocyte protoporphrin, μg/l</td>
<td>555 ± 278</td>
<td>460</td>
<td>200</td>
<td>1,310</td>
</tr>
<tr>
<td>Hemoglobin, g/l</td>
<td>131 ± 8</td>
<td>131</td>
<td>114</td>
<td>155</td>
</tr>
</tbody>
</table>

No. of subjects was 33 except for lean body mass and serum iron where n = 32.
the relationship between plasma Zn and $Q_i$. The broken line
representation of these relationships. The broken line
$\text{H}_i$, 0.99 ± 0.24 0.24 1.01 0.53 1.40
$g_{1i}$, day$^{-1}$ 165 ± 26 0.16 169 112 221
$H_2$, 0.059 ± 0026 0.44 0.061 0.023 0.127
$g_{2i}$, day$^{-1}$ 12.8 ± 4.3 0.34 13.7 3.5 20.8
$H_3$, 0.0156 ± 00036 0.23 0.0159 0.0088 0.0231

| $k_{1i}$, day$^{-1}$ | 154 ± 25 0.16 155 107 214 |
| $k_{12i}$, day$^{-1}$ | 22.1 ± 6.4 0.29 23.0 7.8 35.1 |
| $k_{21i}$, day$^{-1}$ | 64.6 ± 10.8 0.17 65.0 44.5 83.3 |
| $k_{13i}$, day$^{-1}$ | 1.38 ± 0.25 0.13 1.33 0.87 1.90 |
| $k_{31i}$, day$^{-1}$ | 90 ± 25 0.28 92 43 164 |

$Q_i$, µmol 31.8 ± 8.2 0.26 29.7 21.1 49.8
$Q_2$, µmol 110 ± 72.1 0.66 77.4 40.1 307.7
$Q_3$, mmol 2.01 ± 0.50 0.25 1.90 1.24 3.57
EZP, mmol 2.15 ± 0.52 0.24 2.03 1.39 3.65

$F_{21}$, mmol/day 2.06 ± 0.64 0.31 2.04 1.00 4.12
$F_{31}$, mmol/day 2.78 ± 0.88 0.32 2.54 1.43 4.90
Turnover rate, mmol/day 4.84 ± 1.19 0.25 4.63 2.87 8.24

$Q_i$/body wt, µmol/kg 0.505 ± 0.140 0.28 0.467 0.322 0.832
$Q_2$/body wt, µmol/kg 1.78 ± 1.29 0.72 1.37 0.67 5.14
$Q_3$/body wt, µmol/kg 31.4 ± 5.8 0.18 32.5 19.2 42.8
EZP/body wt, µmol/kg 33.6 ± 6.3 0.19 34.0 20.3 44.2

$F_{21}$/body wt, µmol·kg$^{-1}$·day$^{-1}$ 32.8 ± 11.5 0.35 30.3 16.3 68.7
$F_{31}$/body wt, µmol·kg$^{-1}$·day$^{-1}$ 42.8 ± 8.4 0.20 44.9 28.3 64.2
Turnover rate/body wt, µmol·kg$^{-1}$·day$^{-1}$ 75.5 ± 15.0 0.20 72.1 50.1 117.7

$Q_i$/LBM, µmol/kg 0.702 ± 0.017 0.24 0.648 0.474 1.01
$Q_2$/LBM, µmol/kg 2.35 ± 1.52 0.65 1.84 0.98 6.85
$Q_3$/LBM, µmol/kg 44.5 ± 7.9 0.18 45.0 28.2 62.7
EZP/LBM, µmol/kg 47.5 ± 8.4 0.18 47.1 41.6 64.1

$F_{21}$/LBM, µmol·kg$^{-1}$·day$^{-1}$ 45.0 ± 13.1 0.29 45.2 23.9 70.2
$F_{31}$/LBM, µmol·kg$^{-1}$·day$^{-1}$ 61.5 ± 14.7 0.24 59.6 33.9 102.9
Turnover rate/LBM, µmol·kg$^{-1}$·day$^{-1}$ 106.6 ± 21.9 0.21 104.9 70.0 173.0

EZP, rapidly exchangeable zinc pool, a sum of $Q_1$, $Q_2$, and $Q_3$; LBM, lean body mass; RSD, relative standard deviation; $k_{ij}$, transfer rate constant representing fractional transfer into compartment $i$ from compartment $j$; $Q_1$, pool sizes; $F_{ij}$, flux from compartment $i$ to compartment $j$.

$k_{12}$, $k_{31}$, $Q_1$ per lean body mass, and $Q_2$. Figure 3 shows the relationship between plasma Zn and $Q_2$ as a representative of these relationships. The broken line gave the smallest AIC for $g_{1i}$, $g_{2i}$, $k_{11}$, $k_{12}$, $k_{31}$, $Q_1$ per lean body mass, and $Q_2$. Therefore, the broken line was the best equation for $g_{1i}$, $g_{2i}$, $k_{11}$, $k_{12}$, $k_{31}$, $Q_1$ per lean body mass, and $Q_2$ (Table 4). Table 5 shows the coefficients in the broken-line equation. Plasma Zn concentration at the break point of the broken line was found to be 9.94 µmol/l (650 ng/ml; $k_{12}$) to 11.5 (750 ng/ml; $k_{11}$) µmol/l. The relationship between plasma Zn and $Q_2$ ($R^2 = 0.587$) was stronger than other parameters ($R^2 = 0.285–0.483$).

Determination of cutoff value for plasma Zn based on Zn kinetic parameters. Because $g_{1i}$, $g_{2i}$, $k_{11}$, $k_{12}$, $k_{31}$, $Q_1$ per lean body mass, and $Q_2$ changed with plasma Zn, the critical value of plasma Zn to detect low-Zn status was examined based on the correlation between plasma Zn and those parameters. If the estimate of the break point from the plasma Zn-$Q_2$ relationship that was strongest among those parameters is used, the critical value for plasma Zn becomes 10.8 µmol/l (709 ng/ml). The median value of the break points found from those parameters was 11.0 µmol/l (750 ng/ml). The minimum value was 9.94 µmol/l (650 ng/ml) based on $k_{12}$. The maximum value was 11.5 µmol/l (750 ng/ml) based on $k_{11}$. The conventional cutoff value was 10.7 µmol/l (700 ng/ml) for fasting plasma Zn between normal and low places at the middle of the range of break points (9.94–11.5 µmol/l or 650–750 ng/ml).

The critical value for low $Q_2$ was determined as the mean + 2SD for the subjects whose plasma Zn was less
than the break point in the plasma Zn-Q2 relationship. The number of subjects whose plasma Zn was less than the break point (10.8 μmol/l or 700 ng/ml) was 18. Outliers were detected by Grubbs’ test (5). After the removal of one outlier, the mean ± SD of Q2 was 72.5 ± 19.0 μmol (4.74 ± 1.24 mg, n = 17). The critical value for low Q2 was tentatively decided to be 112 μmol or 7.3 mg as a round number of the mean ± 2SD, although further verification is required.

Relationship between plasma Zn and other Zn kinetic parameters. Plasma Zn was significantly correlated with $k_{13}$ ($r = -0.367, n = 33, P = 0.031$) and $F_{21}$ ($r = 0.429, n = 33, P = 0.013$). Plasma Zn significantly correlated with UZnExR ($r = 0.597, n = 24, P = 0.002$), UZnExR per lean body mass ($r = 0.605, n = 24, P = 0.002$), and urinary Zn excretion rate constant ($r = 0.438, n = 24, P = 0.032$). AIC for the relationship of plasma Zn and parameters relating to the urinary Zn excretion were similar among all models (Table 4). A correlation between plasma Zn and EZP per lean body mass was marginally significant ($r = 0.307, n = 32, P = 0.087$). No significant correlation was found between plasma Zn and $Q_3$ per lean body mass ($r = 0.204$), $F_{31}$ per lean body mass ($r = 0.071$), TR per lean body mass ($r = 0.110$), and $k_{21}$ ($r = 0.112$).

Comparison of Zn kinetic parameters and other indexes between normozincemic and hypozincemic subjects. Normozincemia and hypozincemia were respectively defined as plasma Zn greater than or less than/equal to 10.7 μmol/l (700 ng/ml). Sixteen subjects were normozincemic; 17 subjects were hypozincemic. The hypozincemic subjects had higher $g_2$, $k_{12}$, $k_{13}$, and hair Zn than normozincemic subjects. The hypozincemic subjects had lower plasma Zn, $Q_2$, EZP per lean body mass, and UZnExR. Serum Fe concentration of the hypozincemic was significantly less than the normozincemic subjects. The difference of serum ferritin (mean ± SD, μg/l) between the normozincemic (28.6 ± 21.2) and hypozincemic (18.1 ± 9.7) subjects was marginal ($P = 0.086$). Hb concentrations (means ± SD) in blood were not significantly different between the normozincemic and hypozincemic subjects (132 ± 8 vs. 130 ± 9 g/l, $P = 0.96$; Table 6). The hypozincemic subjects had slightly but significantly increased anion gap and sodium in serum.

Electrical taste thresholds. The lower part of Table 6 shows the electrical taste thresholds of normozincemic subjects (plasma Zn >10.7 μmol/l or 700 ng/ml) and hypozincemic subjects (plasma Zn ≤10.7 μmol/l or 700 ng/ml). Hypozincemic subjects had lower thresholds in electric taste detection. The electrical taste detection thresholds <0 dB and 6 dB were considered to be hypersensitivity, respectively, in chorda tympani and glossopharyngeal nerve. Under these tentative criteria, for the left side of chorda tympani, 8 normal and 1

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Table 3. Correlation coefficients between pool sizes and body weight, lean body mass, or plasma Zn concentration

<table>
<thead>
<tr>
<th></th>
<th>Plasma Zn (n = 33)</th>
<th>Body Weight (n = 33)</th>
<th>Lean Body Mass (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
<td>r</td>
</tr>
<tr>
<td>$Q_1$</td>
<td>0.464</td>
<td>0.007</td>
<td>0.311</td>
</tr>
<tr>
<td>$Q_2$</td>
<td>0.675</td>
<td>0.001</td>
<td>-0.093</td>
</tr>
<tr>
<td>$Q_3$</td>
<td>0.114</td>
<td>0.528</td>
<td>0.648</td>
</tr>
<tr>
<td>EZP</td>
<td>0.212</td>
<td>0.236</td>
<td>0.622</td>
</tr>
<tr>
<td>$F_{21}$</td>
<td>0.429</td>
<td>0.013</td>
<td>0.158</td>
</tr>
<tr>
<td>$F_{31}$</td>
<td>-0.100</td>
<td>0.580</td>
<td>0.794</td>
</tr>
<tr>
<td>TR</td>
<td>0.157</td>
<td>0.384</td>
<td>0.673</td>
</tr>
</tbody>
</table>

n, No. of subjects. TR, plasma Zn turnover rate.
Table 4. Comparison of the curve fittings to the relationships between plasma Zn and Zn kinetic parameters using AIC

<table>
<thead>
<tr>
<th>Zn Kinetic Parameters</th>
<th>g₁</th>
<th>g₂</th>
<th>k₁₁</th>
<th>k₁₂</th>
<th>k₁₃</th>
<th>Q₂/LBM</th>
<th>Q₂</th>
<th>UZnExR</th>
<th>UZnExR/LBM</th>
<th>UZnExR Constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>32</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>AIC for curve 1</td>
<td>749</td>
<td>492</td>
<td>746</td>
<td>539</td>
<td>744</td>
<td>624</td>
<td>498</td>
<td>780.6*</td>
<td>406.3</td>
<td>57.3</td>
</tr>
<tr>
<td>AIC for curve 2</td>
<td>379</td>
<td>489</td>
<td>736</td>
<td>536</td>
<td>738</td>
<td>619</td>
<td>489</td>
<td>781.7</td>
<td>405.4*</td>
<td>55.8*</td>
</tr>
<tr>
<td>AIC for curve BL</td>
<td>735*</td>
<td>485*</td>
<td>734*</td>
<td>532*</td>
<td>733*</td>
<td>613*</td>
<td>482*</td>
<td>781.9</td>
<td>406.2</td>
<td>58.1</td>
</tr>
</tbody>
</table>

AIC, Akaike information criteria; UZnExR, urinary zinc excretion rate; UZnExR constant calculated as UZnExR divided by Q₂; curve 1, straight line, the first-order polynomial equation; no. of parameters, 2; curve 2, quadratic curve, the second-order polynomial equation; no. of parameters, 3; curve BL, broken line with a horizontal section, broken-line equation; no. of parameters, 3; For the broken-line equation, $y = a(x - b) + a|x - b| + c$. AIC was calculated as follows: $AIC = n \ln (2\pi a^2) + n + 2(p + 1)$, where $n$ is the no. of data, $\ln$ is the natural logarithmic function, $\pi$ is the ratio of the circumference to the diameter in circles, $a^2$ is the residual sum-of-squares, and $p$ is the no. of parameters. *Smallest AIC.

A hypersensitive subject was normozincemic; 4 normal and 11 hypersensitive subjects were hypozincemic ($P = 0.005$, Fisher’s exact probability). For the right side of chorda tympani, 7 normal and 2 hypersensitive subjects were normozincemic; 4 normal and 11 hypersensitive subjects were hypozincemic ($P = 0.021$). Stimulation of the left side of glossopharyngeal nerve found 8 normal and 9 hypersensitive subjects with normozincemia and 5 normal and 10 hypersensitive subjects with hypozincemia ($P = 0.011$). Stimulation of the right side of the glossopharyngeal nerve found seven normal and one hypersensitive subject with normozincemia and 5 normal and 10 hypersensitive subjects with hypozincemia ($P = 0.026$). The thresholds for tastants were not different (data not shown).

Association between subjects’ histories and the Zn pool size Q₂. Associations of Q₂ (μmol) with food frequencies are shown in Table 7. The significant positive predictors of Q₂ were yogurt and beef. The significant negative dietary predictor was bran breakfast cereal.

DISCUSSION

Plasma has Zn binding capacity of ~5 mg/l compared with the plasma Zn concentration of ~1 mg/l (4). Plasma volume is ~3 liters. Therefore, the total amount of unbound Zn binding capacity is ~12 mg. We administered 2 mg Zn tracer over 3 min to allow enough time for mixing and binding of Zn to the plasma proteins. The obtained Zn kinetic parameters were comparable with reported values. Especially, $k_{11}$ is considered most affected by the dose of Zn because it relates to the initial phase of disappearance. The $k_{11}$ obtained by our study ranged from 107 to 214 day⁻¹. According to King et al. (29), $k_{11}$ increased from ~150 day⁻¹ at baseline to 200 day⁻¹ at the end of depletion. Therefore, we believe the dose of 2 mg Zn should not influence Zn kinetics.

When the plasma volume was calculated as $Q_1$ divided by plasma Zn concentration, it became 2.98 ± 0.71 liters (means ± SD, $n = 33$). The estimated plasma volume in liters from Steinbeck’s formula (55), i.e., $2.742 + 0.02664 (\text{weight in kg} - 57.14) + 0.02759 (\text{height in meters} - 1.639)$, was 2.90 ± 0.46 liters (mean ± SD, $n = 33$). The correlation coefficient between the plasma volume calculated from Zn kinetics and that based on Steinbeck’s formula was 0.446 ($P = 0.009$, $n = 33$). These results are consistent with the nature of compartment 1 as the central compartment, i.e., plasma Zn compartment.

A measurable peripheral compartment by tracer study is a composite of subcompartments with similar kinetic properties. Kinetic parameters do not provide information concerning the anatomy of the compartment. Although the nature of compartment 2 cannot be defined from the data, a certain portion of liver Zn is presumably represented by compartment 2. Wallwork

Table 5. Coefficients in the broken-line equation that describes the nonlinear relationships between plasma Zn and Zn kinetic parameters

<table>
<thead>
<tr>
<th>Zn Kinetic Parameters</th>
<th>g₁</th>
<th>g₂</th>
<th>k₁₁</th>
<th>k₁₂</th>
<th>k₁₃</th>
<th>Q₂/LBM</th>
<th>Q₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Estimate of a</td>
<td>-8.17</td>
<td>-4.38</td>
<td>-6.70</td>
<td>-7.75</td>
<td>-7.52</td>
<td>0.0572</td>
<td>28.5</td>
</tr>
<tr>
<td>ASE of a</td>
<td>2.81</td>
<td>0.39</td>
<td>3.60</td>
<td>0.42</td>
<td>2.81</td>
<td>0.0220</td>
<td>5.9</td>
</tr>
<tr>
<td>Estimate of b</td>
<td>11.0</td>
<td>11.0</td>
<td>11.5</td>
<td>9.94</td>
<td>11.0</td>
<td>11.0</td>
<td>10.8</td>
</tr>
<tr>
<td>ASE of b</td>
<td>0.64</td>
<td>0.58</td>
<td>0.70</td>
<td>0.63</td>
<td>0.67</td>
<td>0.61</td>
<td>0.40</td>
</tr>
<tr>
<td>Estimate of c</td>
<td>173</td>
<td>14.7</td>
<td>160</td>
<td>25.9</td>
<td>97.1</td>
<td>0.653</td>
<td>76.6</td>
</tr>
<tr>
<td>ASE of c</td>
<td>5</td>
<td>0.81</td>
<td>5</td>
<td>1.4</td>
<td>5.0</td>
<td>0.034</td>
<td>11.3</td>
</tr>
<tr>
<td>R²</td>
<td>0.26</td>
<td>0.439</td>
<td>0.285</td>
<td>0.483</td>
<td>5.298</td>
<td>0.292</td>
<td>0.587</td>
</tr>
<tr>
<td>SEE</td>
<td>22.2</td>
<td>3.3</td>
<td>21.9</td>
<td>4.74</td>
<td>21.8</td>
<td>0.145</td>
<td>47.9</td>
</tr>
<tr>
<td>P value</td>
<td>0.003</td>
<td>0.0002</td>
<td>0.0001</td>
<td>0.005</td>
<td>0.007</td>
<td>0.001</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Units are μmol/l. ASE, asymptotic standard error; SEE, standard error of estimate. Letters "a", "b," and "c" denote the coefficients in the broken-line equation: $y = a(x - b) + a|x - b| + c$. Units for a is day⁻¹ [μmol/l] for $g_1$, $g_2$, $k_{11}$, $k_{12}$, and $k_{13}$, μmol/kg/μmol/l for $Q_2$/LBM and μmol/(μmol/l) for $Q_2$. Units for b is μmol/l. Units for c and SEE are day⁻¹ [μmol/l] for $g_1$, $g_2$, $k_{11}$, $k_{12}$, and $k_{13}$, μmol/kg for $Q_2$/LBM and μmol for $Q_2$. P value was determined from the F-ratio test.
et al. (59) observed Zn concentrations in liver and plasma that fluctuated during the feeding cycle of Zn-deprived rats. In association with anorexia, Zn increased in plasma, presumably from tissue catabolism. The relative amplitude of the feeding cycle to the median Zn levels was 65 and 26% for plasma and liver, respectively. Aamodt et al. (1) found the mean radioactivity at the liver region in 17 patients with smell/taste dysfunction patients increased very rapidly to 50% of the total injected amount of $^{65}$Zn within 15 min. Foster et al. (16) designated the fastest-exchanging peripheral compartment to be part of the liver.

In the model of Lowe et al. (35), four compartments in plasma and tissues plus two compartments in the gastrointestinal tract were used to simultaneously fit the tracer-tracee data in plasma, urine, and feces after intravenous and oral doses of Zn tracers over 11 days. In the model of Lowe et al. (35), compartment 2 and 3 were, respectively, designated as “Tissues Fast” and “Tissues Slow.” In the model of Lowe et al. (35), the size of the central compartment was shown as $M_1$; the size of compartment 2 as $M_2$; and the size of compartment 3 as $M_3$. Lowe et al. (35) suggested that these compartments were located within liver, erythrocytes, and kidney based on the comparison of their model and the more complex models of Foster et al. (16) and Wastney et al. (60).

$M_1$ in Lowe’s model and $Q_1$ in the present model were similar as well as $M_2$ and $Q_2$. However, $Q_3$ in the present method was 1.70 times $M_3$ in Lowe’s model; EZP (sum of $Q_1$, $Q_2$, and $Q_3$) was 1.63 times EZP (sum of $M_1$, $M_2$, and $M_3$). Those differences were probably derived from the differences in models used and body weights of the subjects. The ratio of the body weight of Lowe’s subjects to our subjects and the factor derived from the comparison of Lowe’s model to our model were multiplied for estimating $M_3/Q_3$ and EZP (Lowe’s model)/EZP (present model). The outcome was 1.76 ($=1.20 \times 1.47$) for $M_3/Q_3$ and 1.66 for EZP (Lowe’s model)/EZP (present model) ($=1.20 \times 1.38$) (see the supplemental material, available at the American Journal of Physiology: Endocrinology and Metabolism web site). These estimates were similar to the actual numbers found.

Hypozincemic subjects had increased Zn transfer rate constants, decreased Zn pool sizes, and increased hair Zn. Subjects with low plasma Zn concentrations had accelerated plasma Zn tracer disappearance. Rapid plasma Zn tracer disappearance is characteristic of Zn deficiency (44, 70). Comparable results were reported by King et al. (29, 30). They measured Zn kinetic indexes in five healthy men before and after 5–6 wk of severe Zn depletion ($<5 \mu$mol/day). The $k_{11}$ (translated to our notation) increased from $\sim150$ day$^{-1}$ at baseline to 200 day$^{-1}$ at the end of depletion. In our 33 female subjects, $k_{11}$ ranged from 107 to 214 day$^{-1}$, and a negative correlation between $k_{11}$ and plasma Zn was found.

The decreased Zn pool size, $Q_2$, was associated with a food history compatible with lower consumption of bioavailable Zn, i.e., little beef and much bran break-

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### Table 6. Comparison of Zn kinetic and biochemical indexes and electric taste thresholds (shown by the logarithmic scale of the direct current) between normozincemic (plasma Zn $>10.7 \mu$mol/l or 700 ng/ml) and hypozincemic (plasma Zn $\leq 10.7 \mu$mol/l or 700 ng/ml) subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normozincemic</th>
<th>Hypozincemic</th>
</tr>
</thead>
</table>
| $g_2$, day$^{-1}$               | 10.9 ± 5.0    | 14.7 ± 2.5   | 0.012
| $k_{12}$, day$^{-1}$            | 18.8 ± 6.7    | 25.2 ± 4.2   | 0.003
| $k_{13}$, day$^{-1}$            | 1.27 ± 0.22   | 1.48 ± 0.23   | 0.012
| $Q_2$, $\mu$mol                 | 145 ± 89      | 76 ± 26      | 0.008
| EZP per lean body mass, $\mu$mol/kg | 51.1 ± 6.6   | 44.4 ± 8.6   | 0.017
| Urinary Zn excretion rate, $\mu$mol/day | 11.0 ± 8.2 | 4.83 ± 5.67 | 0.038
| Urinary Zn excretion rate constant, day$^{-1}$ | 0.544 ± 0.230 | 0.175 ± 0.121 | 0.045
| Plasma Zn, $\mu$mol/l           | 12.0 ± 1.1    | 9.53 ± 0.78  | 0.001
| Hair Zn, $\mu$mol/g             | 2.06 ± 0.46   | 2.84 ± 0.96  | 0.009
| Serum Fe, $\mu$mol/l            | 16.3 ± 7.9    | 10.1 ± 4.0   | 0.013
| Anion gap, mmol/l               | 11.6 ± 1.8    | 12.9 ± 1.9   | 0.043
| Serum sodium, mmol/l            | 139.4 ± 2.0   | 140.7 ± 1.5  | 0.047

<table>
<thead>
<tr>
<th>Electric taste thresholds</th>
<th></th>
<th></th>
</tr>
</thead>
</table>
| Chorda tympani, left side, dB   | 4 (±6.22)     | 0 (±6.18)    | 0.023
| Chorda tympani, right side, dB  | 2 (±6.22)     | 0 (±6.18)    | 0.029
| Glossopharyngeal nerve, left side, dB | 14 (±4.30) | 2 (±6.22) | 0.016
| Glossopharyngeal nerve, right side, dB | 15 (±4.30) | 0 (±6.26) | 0.097

Values are means ± SD; or median with minimum and maximum values in parentheses, respectively; n, no. of subjects.

### Table 7. Associations of the lesser peripheral Zn pool size $Q_3$ ($\mu$mol) with food frequencies (times/wk) examined by multiple regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regression Coefficient</th>
<th>SE</th>
<th>Partial Correlation Coefficient</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>77.5</td>
<td>16.4</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Yogurt</td>
<td>19.9</td>
<td>6.1</td>
<td>0.537</td>
<td>0.003</td>
</tr>
<tr>
<td>Bran breakfast cereals</td>
<td>−17.4</td>
<td>7.0</td>
<td>−0.438</td>
<td>0.020</td>
</tr>
<tr>
<td>Beef</td>
<td>11.6</td>
<td>5.4</td>
<td>0.386</td>
<td>0.042</td>
</tr>
<tr>
<td>Orange juice</td>
<td>−3.44</td>
<td>1.99</td>
<td>−0.322</td>
<td>0.095</td>
</tr>
</tbody>
</table>

$n = 31$ subjects. $R^2 = 0.372$; SEE = 53.4; $P = 0.013$. 

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fast cereals. UZnExR and plasma Zn were positively correlated. The increased transfer rate constants and the decreased UZnExR and urinary Zn excretion rate constant in hypozincemic women may indicate a possible adaptation mechanism to low intake of bioavailable Zn. However, the hypozincemic subjects had decreased Zn pools. A “sacrificial” adaptation mechanism of compartment 2 may exist when Zn intake is low. In hypozincemia, the transfer rate constants $k_{12}$ and $k_{31}$ were increased; $Q_2$ was decreased; and $Q_1$ remained unchanged. Teleologically, these changes seem to show the shift of Zn from compartment 2 to compartment 3 or some other location outside of the compartment model considered, compensating for the decreased Zn intake. In contrast, the Zn pool size $Q_2$ was not changed within the range where plasma Zn was less than the break point (10.7 μmol/l or 700 ng/ml). A certain amount of Zn may be necessary to maintain the basic function of “some” organs that comprise compartment 2. Although changes were slight, hypozincemic subjects had increased anion gap and sodium concentration in serum. These changes might be related to the slight alteration in the function of Zn as a cofactor for carbonic anhydrase that is responsible for the electrolyte and acid-base balance (32). Zn is known to induce hyperpolarization of membrane potential of clonal rat pancreatic β-cells possibly via its binding to the ATP-sensitive K$^+$ channel (7). Na$^+$-K$^+$-ATPase activity is decreased in sciatic nerves of Zn-deficient guinea pigs (40) and in erythrocytes of Zn-deficient rats (23). Zn is essential for flavokinase activity that influences ATP availability (67).

Our subjects displayed gustatory hypersensitivity to the electric stimulus without apparent abnormality of taste perception. Zn deficiency slows motor and sensory nerve conduction velocity in guinea pigs. This phenomenon is mediated at least in part by decreased Na$^+$-K$^+$-ATPase activity and decreased myo-inositol concentrations in peripheral nerves (40, 57). In humans, Zn deficiency may cause dysesthesia, dysgeusia/ hypogeusia, dysosmia/hyposmia, and muscle weakness (24, 25, 54, 71). Zn-deficient patients do not always recognize dysgeusia. We suggest that hypersensitivity of the gustatory nerves to electrical stimulation might be used to detect mild Zn deficiency. Provisionally, until further verification, the gustatory response to 0 dB and 6 dB electric stimuli may serve as indicators of hypersensitivity of the chorda tympani and glossopharyngeal nerves, respectively.

In this study, the hypozincemic women had higher hair Zn concentrations than the normozincemic women. Several researchers reported that, in adults, hair Zn was increased by Zn deprivation (6, 39, 42). In contrast, children with low-Zn status had depressed hair Zn concentrations (21, 56). These contrasting results may be explained by hair growth rate and Zn supply to growing hairs. Zn deficiency apparently decreases Zn supply from blood to growing hair. Hair growth is inhibited by Zn deficiency (42). In Zn-deficient Merino lambs (65), the wool growth was depressed, whereas the bulb-cell production was not affected. Once hair cells are denucleated, neither Zn nor dry matter is transferred or added. Therefore, the hair Zn concentration equals the Zn supply to hair divided by the hair growth rate. If Zn deprivation decreases the Zn supply to hair more than the hair growth rate, the hair Zn decreases, and vice versa.

Before our work, the conventional cutoff value (10.7 μmol/l or 700 ng/ml) for fasting plasma Zn between normal and low was arbitrary in that it was not based on function. This study found the break points in the relationship between plasma Zn and Zn kinetic parameters. They varied in a similar fashion. This finding provides a biological basis for the cutoff. The estimate of the break point (10.8 μmol/l or 709 ng/ml) for plasma Zn in the plasma Zn–$Q_2$ plot virtually agreed with the conventional cutoff value (10.7 μmol/l or 700 ng/ml) for plasma Zn between normal and low-Zn nutriture. When this conventional cutoff value was used as a delimiting number between normal and low-Zn nutriture, several indexes such as $Q_3$, EZP per lean body mass, electrical taste thresholds, serum iron, and anion gap were changed at this cutoff value. The break points based on the different kinetic parameters ranged from 9.94 μmol/l (650 ng/ml) to 11.5 μmol/l (750 ng/ml). Considering the uncertainty of plasma (or serum) Zn level (18), the “safer” cutoff value might be 11.5 μmol/l (750 ng/ml), although further verification is necessary.

Food items that predicted $Q_2$ were beef, yogurt, and bran breakfast cereals. Beef contains highly bioavailable Zn (17). Consistently, higher frequency of beef consumption was associated with higher $Q_2$. Yogurt contains lactic acid that may increase the solubility of Zn and may subsequently increase Zn absorption. The association between higher consumption of yogurt and higher $Q_2$ is consistent with the characteristics of yogurt. Bran breakfast cereals contain phytate, dietary fibers, and products of nonenzymatic browning that decrease Zn absorption (12–14, 20, 31, 37, 51, 52, 66). Our finding that higher bran breakfast cereals were associated with lower $Q_2$ is consistent with an inhibiting effect of bran on Zn absorption. Although the effect was not statistically significant, higher orange juice consumption was associated with low $Q_2$. Orange juice contains ascorbic acid, which is known to reduce Zn absorption (28). The four food items estimated 37% variance of $Q_2$. This suggests that food frequency questionnaires are practically useful to estimate Zn status.

In conclusion, a nonlinear relationship between plasma Zn and Zn kinetic parameters was found in premenopausal women. The rapidly turning over tissue pool of Zn positively correlated with lean body mass, consistent with the intracellular location of Zn. The positive dietary predictors of the Zn pool $Q_2$ were yogurt and beef; the negative dietary predictor of the Zn pool $Q_2$ was bran breakfast cereal. Premenopausal women who consume limited sources of highly bioavailable Zn or facilitators of Zn retention and excessive sources of Zn absorption inhibitors are likely to be at risk of Zn deficiency. Electrical gustatory nerve stimulation threshold was decreased in poor Zn status. Al-
though such a relationship is known from studies in experimental animals, this is the first demonstration in humans (that we know of).

DISCLOSURES

This study was supported by Department of Defense Army Grant DAMD 17-95-C-5112. The study was conducted in the General Clinical Research Center at the University of Texas Medical Branch at Galveston, funded by grant M01 RR-00073 from the National Center for Research Resources.


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