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ABSTRACT
Background: The deuterated-retinol-dilution technique provides a quantitative estimate of total-body vitamin A (TBVA) stores in adults. To apply the technique to children, information on plasma retinol kinetics in this age group is needed.

Objectives: We described the plasma retinol kinetics of an oral dose of $[^2H_4]$retinyl acetate in a population of Peruvian children (12–24 mo of age) in order to examine the relation between TBVA stores and individual plasma isotopic ratios 3 d after the dose and to estimate 1) the time required for the isotope dose to mix with endogenous vitamin A, 2) the fractional catabolic rate for retinol, and 3) TBVA stores.

Design: An oral dose of $[^2H_4]$retinyl acetate (14 μmol retinol equivalents) was administered to children ($n=107$) to construct a population-level kinetic curve of the plasma ratio of $[^2H_4]$retinol to retinol to estimate equilibration time and the fractional catabolic rate. TBVA stores were estimated by using a modification of the isotopic dilution equation for adults.

Results: The dose of $[^2H_4]$retinyl acetate fully mixed with endogenous vitamin A 8 d after the dose. The fractional catabolic rate was 0.022/d (95% CI: 0.014, 0.030/d). Mean (±SD) TBVA stores were estimated as 0.097 ± 0.081 mmol (range: 0.016–0.392 mmol). Plasma ratios of $[^2H_4]$retinol to retinol 3 d after the dose were correlated with the inverse of estimated TBVA stores ($r = -0.74, P < 0.0001$).

Conclusions: Compared with previous results in adults, the equilibration time occurred earlier and the estimated system fractional catabolic rate was higher in this population of children. The modified isotopic dilution equation provided estimates of hepatic vitamin A concentration that are similar to values reported in US children at autopsy.

KEY WORDS Vitamin A stores, children, stable isotope, vitamin A, plasma kinetics, $[^2H_4]$retinyl acetate, Peru

INTRODUCTION
The deuterated-retinol-dilution (DRD) technique is an indirect method of assessing total body stores of vitamin A (1). The technique consists of administering an oral dose of $[^2H_4]$retinyl acetate to subjects and measuring the plasma isotopic ratio of $[^2H_4]$retinol to retinol after the isotope dose has fully mixed with endogenous vitamin A stores, which requires 20 d in adults (2). Total body stores of vitamin A are estimated on the basis of the principles of isotopic dilution by using a measured postequilibration plasma isotopic ratio of $[^2H_4]$retinol to retinol and a set of assumptions described by Furr et al (1). Briefly, it is assumed that 50% of the isotope dose is retained and that the fractional catabolic rate for retinol in adults is 0.5% per d (1, 3). The DRD technique has been validated in adult surgical patients with low or adequate total body stores of vitamin A by comparing estimates of hepatic vitamin A stores obtained by using the DRD technique with direct measurement of hepatic vitamin A in biopsy specimens obtained at the time of surgery (1, 4). It is estimated that hepatic vitamin A stores account for ≈90% of total body stores of vitamin A in well-nourished individuals (5). The biopsy method estimates hepatic vitamin A stores, and the DRD technique estimates total body stores of vitamin A. Although a comparison of results obtained by the 2 techniques is not ideal, an estimate of hepatic vitamin A stores is considered to be the best indicator of vitamin A status, and it is the only method that provides a quantitative estimate of vitamin A stores. Results of these studies indicate that the technique provides a good quantitative estimate of mean hepatic vitamin A stores for groups of adult subjects. The DRD technique has also been shown to detect quantitative changes in total body stores of vitamin A in response to supplementation with different amounts of unlabeled vitamin A (6). These results suggest that the DRD technique may be useful for assessing the efficacy of vitamin A intervention programs in populations in whom vitamin A deficiency is endemic by estimating the mean change in total body stores of vitamin A in response to the intervention.

Because vitamin A intervention programs are commonly directed toward preschool-aged children, it is necessary to determine whether the DRD technique is useful for evaluating the efficacy of interventions in this age group. Initially, information on the plasma kinetics of an oral dose of $[^2H_4]$retinyl acetate in this age group is required to determine whether the isotopic dilution equation (1) that is used to estimate total body stores of vitamin A in adults needs to be modified when applied to a population of children. Specifically, information on the optimal time for obtaining measurements of the plasma isotopic ratio of $[^2H_4]$retinol to...
retinol for estimation of vitamin A stores and an estimate of the fractional catabolic rate for retinol in this age group are needed.

The purpose of the present study was to describe the plasma kinetics of an oral dose of \(^{1}H\)retinyl acetate among a population of preschool-aged children to determine the time at which the dose fully mixes with endogenous body stores of vitamin A and to estimate the fractional catabolic rate of retinol. In addition, because data from studies in rats indicate that early postdose measurements of isotope enrichment in plasma are highly predictive of total body stores of vitamin A (7), plasma isotopic ratios 3 d after the dose were compared with subsequent estimates of total body stores of vitamin A.

SUBJECTS AND METHODS

Subjects

The purpose of the study was described to community leaders, health-post personnel, and parents of children between 12 and 24 mo of age in the rural community of Palcamayo and surrounding villages in the Central Peruvian highlands. Written informed consent was obtained from parents who chose to enroll their children in the study. Initially, the children were weighed and measured and examined by a physician. Those children who were without clinical symptoms or signs of vitamin A deficiency, were afebrile, and had been free from diarrhea for 7 d were eligible for the study. Children with mild upper respiratory illness were allowed to participate. All study procedures were approved by the Human Subjects Review Committee of the University of California, Davis, and by the Ethical Review Committee of the Instituto de Investigación Nutricional, Lima, Perú, and included questions about foods that are typically consumed by young children in the Andean regions of Peru.

Procedures

An oral dose of 14 \(\mu\)mol retinol equivalents \(^{1}H\)retinyl acetate (isotopic purity: 98%; Cambridge Isotopes, Andover, MA) was administered to each child, followed by \(\approx 4\) teaspoons of yogurt that had been mixed with 2 teaspoons of corn oil to enhance absorption of the dose. The isotope was dissolved in corn oil (20 mg retinol equivalents/mL) and stored in a glass vial wrapped in foil at \(-20^\circ\)C. Before administering a dose, the isotope solution was thawed at room temperature and protected from light. A positive displacement pipet (Microman pipet; Gilson Medical Electronics, Villiers-le-Bel, France) was used to deliver 200 \(\mu\)L directly into the child’s mouth. Because a large number of blood samples (\(\approx 22\) over a 75-d period) are required to construct a plasma kinetic curve for an individual child, we chose to construct a population-level plasma kinetic curve for the full population of subjects rather than subject the children to repeated blood draws. For the development of the population-level kinetic curve, 2 blood samples were drawn from each child for measurement of the plasma isotopic ratio of \(^{1}H\)retinol to retinol. Each child was scheduled to have a venous blood sample (5 mL) drawn 3 d after administration of the isotope and another sample drawn at 1 of 23 scheduled time points over the 75-d study period. Children were assigned to time points so that there were \(\approx 5\) children at each of the 23 time points. Plasma isotopic ratios were measured at 24 total time points: 2, 3, 4, 5, 6, 8, 24, and 32 h and days 2, 3, 4, 5, 6, 7, 8, 10, 12, 15, 18, 23, 29, 35, 42, and 75. Blood samples (5 mL) were collected by venipuncture into blood collection tubes containing EDTA as an anticoagulant (Becton Dickinson Vacutainer Systems, Franklin Lakes, NJ). Plasma was separated by centrifugation for 10 min at 2800 \(\times g\) and \(\approx 25^\circ\)C, aliquotted into cryovials, and stored at \(-20^\circ\)C. All of the procedures were conducted in dim light, and plasma samples were covered in foil. Plasma samples were carried by hand on dry ice to the University of California at Davis and were stored at \(-20^\circ\)C until analyzed.

Frequency of intake of vitamin A–rich foods

A food-frequency questionnaire consisting of questions about 32 vitamin A–rich foods was administered to mothers of participating children to estimate the children’s frequency of consumption of these foods. Information on portion size was not collected. The purpose of collecting these data was to describe the pattern of intake of vitamin A–rich foods among the participating children at the time of the study. The food-frequency questionnaire was developed by a dietitian at the Instituto de Investigación Nutricional, Lima, Perú, and included questions about foods that are typically consumed by young children in the Andean regions of Peru.

Laboratory procedures

Plasma isotopic ratios of \(^{1}H\)retinol to retinol were determined by gas chromatography–mass spectrometry as previously described (8). Plasma retinol concentrations were measured by HPLC (9). Plasma C-reactive protein (CRP) concentrations were measured by using a commercial radial immunodiffusion kit (Nanorid; The Binding Site, Birmingham, United Kingdom).

Kinetic analysis

The plasma kinetic data were plotted as isotope enrichment: \([^{1}H]\)retinol/(\([^{1}H]\)retinol + retinol) versus time. Equilibration time was determined by fitting to the observed plasma kinetic data an exponential model of the form

\[
\frac{[^{1}H]_{\text{retinol}}}{[^{1}H]_{\text{retinol}} + \text{retinol}} = a_{0}\exp(-b_{1}t) + a_{0}\exp(-b_{2}t) + a_{0}\exp(-b_{3}t)
\]

where \(t\) is time in days. The point at which >95% of the fraction of isotope in plasma was represented by the final exponential term was defined as the equilibration time. (The term equilibration time is used; however, it is recognized that the oral dose does not truly equilibrate with endogenous body stores because of catabolism of labeled vitamin A during the equilibration period and because of the continuous intake of unlabeled vitamin A in the diet.) The fractional catabolic rate for retinol was estimated as the second coefficient \(b_{2}\) of the final exponential term in Equation 1.

Total body stores of vitamin A were estimated by modifying the isotope dilution equation for adults (1) by replacing the fractional catabolic rate of 0.005/d, which is used for adults, with the observed fractional catabolic rate for this population of children. It is assumed that the estimated fractional catabolic rate for the population of children is appropriate for estimating total body stores of vitamin A in individual subjects.

The plasma isotopic ratio of \(^{1}H\)retinol to retinol on day 3 was compared with estimates of total body stores of vitamin A by using regression analysis as described below. This comparison was possible only for those subjects with plasma isotopic ratio measurements both at day 3 and after the equilibration.

Statistical analysis

Student’s \(t\) test was used for comparisons of plasma retinol concentrations with estimated vitamin A pool size in children with a
normal or elevated (> 10 mg/L) plasma CRP concentration and for comparisons of estimated vitamin A pool size in children who were or were not receiving breast milk. Regression analysis was used to predict the estimated vitamin A pool size from plasma isotopic ratios of [2H4]retinol to retinol on day 3. The data were examined empirically, and among the various transformations of the x and y variables (no transformation, inverse, logarithm, powers), the best correlation was achieved between the day 3 plasma ratio of [2H4]retinol to retinol and the inverse of the estimated vitamin A pool size. All statistical analyses were performed with SAS software (release 6; SAS Institute Inc, Cary, NC).

RESULTS

Subjects

A total of 107 children (62 males, 45 females) from 12 to 24 mo of age participated in the study. Because of difficulty in locating the children on the days that they were scheduled to have blood drawn, blood samples both at 3 d after the dose and at 1 of the other 23 time points were obtained from only 38 children. The number of children that provided blood at the 23 time points ranged from 3 to 5 children per time point.

The anthropometric characteristics of the children are shown in Table 1. Growth stunting was prevalent: 57% of the children had height-for-age z scores > 2 SDs below the mean of reference data from the National Center for Health Statistics (10).

Frequency of consumption of vitamin A–rich foods

At the time of the food-frequency questionnaire, mothers of 82 children (76%) reported that they were providing breast milk to their children. Among the children not consuming breast milk, the mean (±SD) frequency of consumption of nonhuman milk was 3.0 ± 3.3 d/wk. The mean weekly frequency of consumption of vitamin A–rich foods by breast-fed and non-breast-fed children is shown in Table 2. The sources of preformed retinol that were consumed most frequently on a weekly basis (> 2 d/wk) were breast milk, butter, and egg. The most frequently consumed sources of provitamin A carotenoids (> 2 d/wk) were carrots, dried chilies, and yellow squash. The most frequently consumed source of added dietary fat was vegetable oil (> 6 d/wk). There was no significant difference in mean total weekly servings of vitamin A–rich foods (including breast milk) between the children who received breast milk and those who did not (47 and 53 servings/wk, respectively; P = 0.28).

However, the mean total weekly servings of retinol-rich foods (excluding breast milk) were significantly higher among the non-breast-fed children than among the breast-fed ones (11 compared with 7 servings/wk; P = 0.02), and the mean total weekly servings of carotene-rich foods were also significantly higher among the non-breast-led children than among the breast-fed ones (42 compared with 27 servings/wk; P = 0.002).

Plasma retinol and C-reactive protein concentrations

Retinol concentrations were measured in plasma samples that were obtained for measurement of plasma isotopic ratios during the 75-d study period. Because it was not always possible to obtain 5 mL blood, there was not enough plasma from some of the children (n = 11) to measure retinol concentrations. When there was sufficient plasma in both of the samples obtained from a child at each of their 2 assigned time points, the retinol concentration was measured in both samples and the average value was reported. The mean (±SD) plasma retinol concentration was 0.80 ± 0.28 μmol/L (range: 0.37–1.92 μmol/L; n = 96). The prevalence of low plasma retinol concentrations (< 0.70 μmol/L) was 31.3%, and the percentage of children with a concentration < 0.52 μmol/L was 10.4%.

Plasma CRP concentrations were measured in 80 children. There was insufficient plasma to measure CRP in the remaining children. Mean plasma retinol concentrations were not significantly different in children with normal or elevated (> 10 mg/L) CRP concentrations (Table 3). (For this comparison, values for the plasma retinol and CRP concentrations were obtained from the same plasma samples.) Nearly 50% (n = 39) of the children had a

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mo)</td>
<td>18.1 ± 4.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>9.4 ± 1.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>74.9 ± 4.5</td>
</tr>
<tr>
<td>Height-for-age z score</td>
<td>-2.18 ± 0.94</td>
</tr>
<tr>
<td>Weight-for-age z score</td>
<td>-1.52 ± 0.93</td>
</tr>
<tr>
<td>Weight-for-height z score</td>
<td>-0.32 ± 0.92</td>
</tr>
</tbody>
</table>

Footnote: *T ± SD; n = 107.

### Table 2

<table>
<thead>
<tr>
<th>Food</th>
<th>Children receiving breast milk (n = 82)</th>
<th>Children not receiving breast milk (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total servings of vitamin A–rich foods</td>
<td>46.7 ± 12.8</td>
<td>52.9 ± 15.9</td>
</tr>
<tr>
<td>Total servings of retinol-rich foods (excluding breast milk)</td>
<td>6.5 ± 4.3</td>
<td>11.1 ± 6.1</td>
</tr>
<tr>
<td>Total servings of carotene-rich foods</td>
<td>26.7 ± 10.2</td>
<td>41.8 ± 14.7</td>
</tr>
</tbody>
</table>

Footnote: *T ± SD. The mean (±SD) ages of the children receiving breast milk and of the children not receiving breast milk were 16.9 ± 4.1 and 18.1 ± 3.1 mo, respectively. Values in the same row with different superscript letters are significantly different, P ≤ 0.02.
TABLE 3
Plasma retinol concentrations in children with or without an elevated C-reactive protein concentration

<table>
<thead>
<tr>
<th>Plasma C-reactive protein</th>
<th>Plasma retinol (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 10 mg/L (n = 41)</td>
<td>0.81 ± 0.25</td>
</tr>
<tr>
<td>&gt; 10 mg/L (n = 39)</td>
<td>0.81 ± 0.37</td>
</tr>
</tbody>
</table>

*See note. There was no significant difference between the groups.

CRP concentration > 10 mg/L [range: 11–66 mg/L; one child had a concentration that exceeded the maximal detectable concentration of the analytic kit (81 mg/L) and was included in the statistical analyses]. Most of the children with an elevated CRP concentration had values between 11 and 19 mg/L (n = 31); 8 children had a CRP concentration > 19 mg/L.

**Estimation of equilibration time**

The exponential equation that best fit the plasma kinetic data is shown in Figure 1. By day 8, 95% of the fraction of isotope dose in plasma was represented by the final exponential term of the equation, and by day 12, 99.5% of the fraction of isotope dose was represented by the final exponential term. The oral dose of \(^{[2H_4]}\)retinyl acetate fully mixed with endogenous vitamin A body stores within 8–12 d after administration of the dose.

**Estimation of fractional catabolic rate**

The system fractional catabolic rate was estimated as 0.022/d (95% CI: 0.014, 0.030/d) by using the second coefficient (slope) of the final exponential term of the exponential equation that was fit to the plasma kinetic data. This corresponds to a half-life of 32 d.

**Estimation of total body stores of vitamin A**

Postequilibration plasma isotopic ratios in subjects who had blood drawn on day 10 or thereafter (n = 43) were used to estimate total body stores of vitamin A by using the isotope dilution equation (1) and the estimated system fractional catabolic rate for this population (ie, 0.022/d). The mean (± SD) total body store of vitamin A estimated by this procedure was 0.097 ± 0.081 mmol (range: 0.016–0.392 mmol). Mean estimated vitamin A pool sizes were not significantly different in children with normal or elevated CRP concentrations (0.087 ± 0.05 and 0.080 ± 0.049 mmol, respectively; P = 0.36; n = 24). The mean estimated vitamin A pool size in breast-fed children tended to be higher than that in non-breast-fed children (0.096 ± 0.069 compared with 0.055 ± 0.027 mmol, respectively; n = 39), although this difference was not significant (P = 0.08). There were no significant relations between anthropometric indicators and estimated vitamin A stores (height/age: r = −0.06, P = 0.7; weight/age: r = −0.16, P = 0.3; weight/height: r = −0.16, P = 0.3) or between plasma retinol concentrations and estimated vitamin A stores (Figure 2; r = −0.25, P = 0.13). Similarly, there were no significant relations between the total number of servings of vitamin A–rich foods (r = −0.21, P = 0.19), retinol-rich foods (r = −0.19, P = 0.22), or carotenereich foods (r = −0.25, P = 0.12) and estimated vitamin A stores.

**Plasma isotopic ratios on day 3 and estimated vitamin A stores**

The relation between plasma isotopic ratios of \(^{[2H_4]}\)retinol to retinol on day 3 and estimated total body stores of vitamin A is shown in Figure 3 for the 12 children with sufficient information. This comparison could only be made in 12 children who had plasma isotopic ratios measured on both day 3 and day 10 or later (after equilibration). Total body stores of vitamin A were cal-
culated as described above by using a postequilibration plasma isotopic ratio and the estimated system fractional catabolic rate for this population. The best prediction equation \( r = -0.74, P < 0.0001 \) was

\[
\text{Estimated total body stores of vitamin A} = \frac{1}{6.08 + 44.88 \times [^{2}H_{4}]\text{retinol:retinol on day 3}}
\]

The prediction equation derived from this comparison was applied to the isotopic ratio data on day 3 for all children who had blood drawn at that time point (\( n = 38 \)) to estimate total body stores of vitamin A for this population of children. With the use of this procedure, the mean \( (\pm SD) \) total body store of vitamin A was 0.091 \( \pm 0.027 \) mmol \((\text{range: } 0.023-0.133 \) mmol). This estimate was compared with the estimate of mean total body stores of vitamin A based on the modified isotope dilution equation. For this comparison, total body stores of vitamin A were estimated for 31 of the 43 children with postequilibration plasma isotopic ratios by using the modified isotopic dilution technique. The 12 children who had plasma isotopic ratio measurements both on day 3 and after equilibration were excluded from the latter estimate because they were included in the estimate of mean total body stores of vitamin A that was based on the plasma isotopic ratios on day 3 and the use of the prediction equation. The mean predicted estimate of total body stores of vitamin A based on the isotopic ratio measurements on day 3 was not significantly different from the mean estimate based on the modified isotope dilution equation \( [0.091 \pm 0.027 \text{ mmol} (n = 38) \) compared with \( 0.104 \pm 0.091 \text{ mmol} (n = 31); P = 0.33] \). There was no significant relation between the predicted estimates of total body stores of vitamin A and plasma retinol concentrations \( r = 0.02, P = 0.93 \).

**DISCUSSION**

The plasma retinol kinetics of an oral dose of \([^{2}H_{4}]\text{retinyl acetate was described in a population of preschool-aged, Peruvian children to determine whether the isotope dilution equation that is used for adults requires modification when applied to young children. The results indicate that the estimated equilibration time for preschool-aged children (8 d) is considerably less than that reported for adults (20 d) and also less than that reported previously for a single healthy, 6-y-old US child (14 d) (2). Data from the present study indicate that plasma isotopic ratio measurement on days 8–12 or later would be appropriate for estimating total body stores of vitamin A in this age group by using the modified DRD technique.**

The estimated system fractional catabolic rate of vitamin A for the population of preschool-aged children was 0.022/d \((95\% \text{ CI: } 0.014, 0.030/d)\), which is \( \approx 4 \) times that estimated for adults \((0.005/d) \) (3). The system fractional catabolic rate may have been affected by several factors in the study population. It is likely that to support growth, children aged 12–24 mo utilize vitamin A at a faster rate than do adults. Thus, the higher rate in children may reflect greater utilization of the vitamin. Infection is another factor that may have affected the vitamin A turnover rate in this population, given that children with mild upper respiratory infections were allowed to participate in the study and that plasma CRP concentrations were elevated in \( \approx 50\% \) of the children. Healthy children may have a fractional catabolic rate closer to the lower confidence limit of 0.014/d observed for this population, or perhaps even lower, approaching the adult level of 0.005/d. However, the fractional catabolic rate for healthy children is still likely to be higher than that of adults because of the presumed higher rate of utilization of the vitamin to support growth. Vitamin A pool size can also affect the fractional catabolic rate. Green et al (7) showed that the fractional catabolic rate is significantly lower in rats with very small or marginal vitamin A pool sizes \((0.0006 \mu g/liver and 0.010 \mu mol/liver, respectively)\) than in rats with large \((0.203 \mu mol/liver)\) vitamin A pool sizes. The retinol disposal rates for these animals also differed significantly by vitamin A pool size. The lower retinol disposal rate in rats with small or marginal pool sizes presumably allows for conservation of vitamin A, whereas the higher disposal rate in rats with large pool sizes presumably prevents accumulation of too much vitamin A in the liver. The difference in retinol disposal rates between rats with marginal or large vitamin A pool sizes was attributed to a difference in the fractional catabolic rate between the groups. In the population of children studied in the present study, the estimated mean vitamin A pool size is considered adequate \((\text{median liver concentration: } 0.224 \mu mol/g)\). It is possible that the fractional catabolic rate may vary in populations of children with lower or higher vitamin A pool sizes. Thus, the fractional catabolic rate estimated for the population of children studied is likely to be typical of the rate among children with adequate vitamin A pool sizes who experience frequent mild infections in low-income communities in developing countries.

Total body stores of vitamin A were estimated as \( \approx 0.097 \text{ mmol}, \) on average, by using the modified DRD technique. The hepatic vitamin A concentration is considered the reference standard for assessing vitamin A stores. Although this information is not available for these children, we can estimate the mean hepatic vitamin A concentration in the study participants and compare that with previously reported values for children of the same age at autopsy.

With the use of an estimate of liver weight for these children \((0.03 \times \text{body wt})\) and an assumption that 90% of total body vitamin A is stored in the liver, the mean \((\pm SD)\) liver vitamin A concentration can be estimated as \( 0.310 \pm 0.259 \mu mol/g \) (median: \( 0.224 \mu mol/g; \) range: \( 0.051–1.24 \mu mol/g)\). This estimate is similar to the reported mean hepatic vitamin A concentration of \( 0.273 \pm 0.150 \mu mol/g \) (median: \( 0.227 \mu mol/g; \) range: \( 0.056–0.504 \mu mol/g)\) in US children aged 1–2 y at autopsy (11) and is higher than the reported mean hepatic vitamin A concentration of \( 0.120 \pm 0.100 \mu mol/g \) (median: \( 0.098 \mu mol/g)\) in Brazilian children aged 1–2 y at autopsy (12). Thus, the estimated liver vitamin A concentrations in the Peruvian children, as assessed by the DRD technique, are within the range of previously reported values for children aged 1–2 y.

The isotopic ratio of \([^{2}H_{4}]\text{retinol to retinol on day 3 provided a fairly good estimate of mean total body stores of vitamin A for this population. This is in agreement with previous observations in rats that indicate that the fraction of isotope dose in plasma shortly after an oral dose is predictive of total body stores of vitamin A (7), and also with previous observations in Filipino schoolchildren that indicate that the plasma isotopic ratio of \([^{2}H_{4}]\text{retinol to retinol on day 3 can be used to detect qualitative changes in vitamin A pool size in response to supplementation with plant carotenoids (13). The relation between the plasma isotopic ratio on day 3 and estimated total body stores of vitamin A was best described by using the transformation of } y = 1/(a + bx). Although this provided the best fit for the data obtained from the population of children studied, the relation between the plasma isotopic ratio on day 3 and estimated total body stores of vitamin A needs to be examined further in future studies.
On the basis of the DRD technique, this population of preschool-aged children was characterized as having adequate body stores of vitamin A. However, the plasma retinol data suggest that subclinical vitamin A deficiency was prevalent. Although none of the children had a plasma retinol concentration < 0.35 μmol/L, 10.4% had a concentration < 0.52 μmol/L, and 31.3% had a concentration < 0.70 μmol/L, which is the cut-off for subclinical deficiency. Mild upper respiratory infections were common in this group of children, and ≈50% had an elevated CRP concentration. Thus, it is possible that plasma retinol concentrations were depressed because of infection. However, plasma retinol concentrations were similar in the children with normal or elevated plasma CRP concentrations. It is also possible that low plasma retinol concentrations are normal for this age group. The normal range for plasma retinol concentrations for children aged 12–24 mo is unknown; thus, values in the ≥0.52–0.70-μmol/L range may not indicate subclinical vitamin A deficiency.

In summary, the data reported in the present study indicate that the vitamin A fractional catabolic rate is higher in this population of Peruvian children with mild respiratory infections than in adults and corresponds to a half-life of ≈32 d. With the use of the fractional catabolic rate observed in this study, the DRD technique provided a quantitative estimate of total body stores of vitamin A that is similar to previously reported values for US children of the same age. Plasma isotopic ratios on day 3 were predictive of total body stores of vitamin A in this population.

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