Magnesium requirements: new estimations for men and women by cross-sectional statistical analyses of metabolic magnesium balance data

Curtiss D Hunt and LuAnn K Johnson

ABSTRACT

Background: Current recommendations for magnesium requirements are based on sparse balance data. The data available to estimate the magnesium average requirement are extremely limited. For example, the magnesium EARs for adult women of all ages are based nearly exclusively on the findings from one study (7) of adults who consumed self-selected diets in a free-living environment. Because the magnesium intakes of American adults are below the EAR, further research is warranted that tests the appropriateness of the current EAR. Estimations of magnesium adequacy typically use balance studies in which positive magnesium balance is associated with adequacy (8–11). However, individual magnesium balance studies seldom test >2 magnesium intakes, such that titration of the magnesium requirement is not possible. Magnesium intakes around predicted zero balance are needed to model the precise relation between mineral intake and loss and retention near zero balance (12).

Results: The models predicted neutral magnesium balance (defined as magnesium output (Y) equal to magnesium intake (M)) at magnesium intakes of 165 mg/d (95% prediction interval (PI): 113, 237 mg/d; Y = 19.8 + 0.880 M; 2.36 mg · kg⁻¹ · d⁻¹ (95% PI: 1.58, 3.38 mg · kg⁻¹ · d⁻¹); Y = 0.306 + 0.870 M), or 0.075 mg · kcal⁻¹ · d⁻¹ (95% PI: 0.05, 0.11 mg · kcal⁻¹ · d⁻¹; Y = 0.011 + 0.857 M). Neither age nor sex affected the relation between magnesium intake and output.

Conclusion: The findings suggest a lower magnesium requirement for healthy men and women than estimated previously.

Differential analysis of the NHANES 1999–2000 data set (3) indicated that the mean magnesium intake for American women (white) aged 51–70 y was 238 mg/d (1). For Mexican and African American women of the same age group, magnesium intakes were lower: 185 and 169 mg/d, respectively (4). For white, Mexican, and African women, intakes were lower still for those reporting no use of dietary supplements: 222, 176, and 150 mg/d, respectively.

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INTRODUCTION

Most Americans consume less than the estimated average requirement (EAR) for magnesium (1) as determined by analysis of the National Health and Nutrition Examination Survey (NHANES) 2001–2002 data set (2). For example, 64% of women aged 51–70 y do not attain the magnesium EAR for that sex-age group (265 mg/d) (1). Instead, their estimated mean magnesium intake during the NHANES 2001–2002 survey was 246 mg/d.
feeding studies conducted at the US Department of Agriculture, Agricultural Research Service, Grand Forks Human Nutrition Research Center, Grand Forks, ND, between 1976 and 2001. The studies were designed originally to determine specific outcomes of nutritional challenges on physiologic function. Twenty-seven of 42 studies (13–35) measured magnesium balance and incorporated design components, such as a control (nutritionally replete) dietary period, relevant for estimating the magnesium requirement by cross-sectional statistical analysis. A broad range of magnesium intakes were used to estimate the amount of dietary magnesium needed to maintain zero magnesium balance in healthy persons.

SUBJECTS AND METHODS

Common design characteristics of the 27 individual original metabolic studies used in the present study are summarized below. Details about each study are available in the references cited in Table 1.

Subjects

Each of the original metabolic studies (Table 1) was reviewed and approved separately by the University of North Dakota Protection of Human Subjects Committee (studies 1-6) or the University of North Dakota Institutional Review Board (studies 7-27 and the current study). Subjects were informed verbally and in writing about the purpose and design for each original metabolic study and provided written informed consent to participate in protocols that followed the guidelines of the Declaration of Helsinki about the use of human subjects.

Recruitment

In all studies, healthy women and men were recruited by public advertisement and selected to enter each study after they were informed in detail of the nature of the research, including the risks and benefits.

Inclusion criteria

Healthy subjects were screened onsite and selected on the basis of medical data (no evidence of alcoholism; normal bone, kidney, thyroid, and liver functions; normal blood pressure and fasting glucose; no chronic medication use; negative lung scan), psychological history (free of psychopathology as determined by the Minnesota Multiphasic Personality Inventory (NCS Assessment, Minneapolis, MN) and an extensive in-house psychological history questionnaire and clinical interview), and diet history (no pertinent food allergies or refusal to eat required foods). Each postmenopausal woman agreed either to discontinue hormone replacement therapy (HRT) before joining a specific study if she and her physician agreed that it was not harmful to stop the HRT or to maintain HRT throughout the study.

Living environment

Accepted male \( n = 93 \); weight (\( \bar{x} \pm SD \)): 76.3 ± 12.5 kg; age: 28.1 ± 8.1 y (range: 19–65 y) and female \( n = 150 \); weight: 71.6 ± 16.5 kg; age: 51.3 ± 17.4 y (range: 19–77 y) subjects resided for the entire length (typically 6 m) of the individual studies in the metabolic ward at the Grand Forks Human Nutrition Research Center. Subject ethnicity was predominantly white (\( n = 227 \)) with additional participation by blacks (\( n = 6 \)), American Indians or Alaskans (\( n = 5 \)), Asians (\( n = 2 \), Hispanics (\( n = 2 \), and undeclared ethnicity (\( n = 1 \)). The ward provided an environment for strict control of food consumption, physical activity, and data collection. Each subject was provided with a private bedroom with cable television, radio with wake-up alarm, intercom to a 24-h central nurse station, telephone, and a semi-private bathroom. Activity areas and the nurse station were adjacent to the private bedrooms. Subjects were allowed to leave the immediate living or dining areas or facility only when accompanied by a chaperone to ensure compliance with study protocols. Meal consumption was observed by specially trained dietary staff members, and irregularities were recorded. Subjects agreed to use only personal care products and in the amounts approved by the principal investigators and to limit and standardize extraneous chemical exposure. Subjects were not allowed to use tobacco or medicinal marijuana or consume alcohol (except for specified ethanol tolerance tests). For most studies, individually prescribed physical activity was performed multiple times per week to maintain initial body composition and physical work capacity.

Diet

Composition

Basal diets were composed of ordinary Western foods, sometimes supplemented with experimental foods (eg, fructose cornbread, egg white drinks, casein biscuits), and fed as a 6-d (study 1) or 3-d (studies 2-27) menu rotation to provide variety, but in a manner that assured variations in nutrient intake were not consequential. Standard temperatures and cooking times were adhered to for each recipe on the menu cycles. Salt and pepper were served in constant amounts, selected by each volunteer, throughout individual studies. The limited menus were supplemented as needed with some nutrients in constant amounts to maintain nutritional adequacy. Because the study intervals included winter months in North Dakota, when sunlight exposure is limited, all subjects received a daily supplement of cholecalciferol (10 or 20 \( \mu g \)). Dietary iron (as ferrous gluconate) was provided in excess of the recommended dietary allowance to mitigate the decline in iron status as a result of phlebotomy during the studies.

Preparation and use

Subjects consumed only and all foods, beverages (including water), and vitamin, mineral, or other supplements provided by the center. The minimum length of any dietary period for any study was 18 d. Whenever possible, food was purchased in single lots sufficient to last for several months to ensure minimal variation in food types. All food was weighed proportionally, selected by each volunteer, through constant amounts, refused by the subjects with the aid of spatulas and rinse bottles. Deionized water was consumed ad libitum. Initial energy requirement for each subject was determined by using the Harris and Benedict equation (37) and adding a uniform amount (between 50% and 70%) of basal energy expenditure for normal physical activity. Except for the weight loss studies (studies 20 and 24), energy intake was adjusted in standardized increments [typically 0.84 MJ (200 kcal)] during the course of each experiment to maintain body weight (measured daily) within ±2% of admission weight. This study used balance
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<th>Study no., study design, and reference</th>
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<td>1. Plant fiber: bioavailability of minerals in food (13)</td>
<td>5/76–2/82 M</td>
<td>M</td>
<td>25.6 ± 8.8 (19.0–52.0)</td>
<td>78.5 ± 15.2 (58.9–135.8)</td>
<td>177.1 ± 7.6 (152.8–193.4)</td>
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<td>27.1 ± 10.3 (19.0–52.0)</td>
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<td>2. Dietary fiber: stool output (14)</td>
<td>5/77–12/80 M</td>
<td>M</td>
<td>29.6 ± 11.1 (19.0–64.0)</td>
<td>77.4 ± 12.3 (60.3–107.9)</td>
<td>176.4 ± 9.3 (152.9–194.7)</td>
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<td>33.9 ± 14.6 (19.0–64.0)</td>
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<td>3. Copper intake: copper balance, absorption, and indicators of status (15)</td>
<td>1/80–12/82 M</td>
<td>M</td>
<td>24.6 ± 4.8 (19.0–32.0)</td>
<td>79.1 ± 10.2 (69.0–105.0)</td>
<td>175.5 ± 5.2 (164.6–182.1)</td>
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<td>24.6 ± 4.8 (19.0–32.0)</td>
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<td>4. Zinc intake: whole-body surface loss of zinc (16)</td>
<td>7/79–9/83 M</td>
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<td>30.9 ± 9.9 (19.0–57.0)</td>
<td>69.4 ± 10.7 (58.3–97.2)</td>
<td>172.2 ± 5.3 (164.1–182.9)</td>
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<td>36.7 ± 18.0 (23.0–57.0)</td>
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<td>5. Physical performance and carbohydrate and lipid metabolism (17)</td>
<td>9/80–12/80 M</td>
<td>M</td>
<td>23.7 ± 6.4 (20.0–31.0)</td>
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<td>6. Brownded and unbrowned corn products: bioavailability of zinc (18)</td>
<td>1/81–4/81 M</td>
<td>M</td>
<td>35.3 ± 20.1 (22.0–65.0)</td>
<td>73.9 ± 6.9 (68.0–83.7)</td>
<td>176.4 ± 9.4 (165.0–186.4)</td>
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<td>35.3 ± 20.1 (22.0–65.0)</td>
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<td>7. Intrinsically and extrinsically labeled meals: $^{65}$Cu absorption (19)</td>
<td>10/82–12/84 M</td>
<td>M</td>
<td>27.2 ± 9.1 (19.0–49.0)</td>
<td>67.9 ± 6.4 (57.5–80.1)</td>
<td>174.7 ± 4.6 (167.7–184.0)</td>
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<td>27.2 ± 9.1 (19.0–49.0)</td>
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<td>8. Fat, vitamin E, and zinc intakes: copper and iron absorption and retention$^6$</td>
<td>7/82–6/83 M</td>
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<td>28.3 ± 5.7 (22.0–37.0)</td>
<td>76.2 ± 14.5 (48.3–91.0)</td>
<td>177.4 ± 7.3 (165.4–189.2)</td>
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<td>28.0 ± 6.1 (22.0–37.0)</td>
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<td>9. Dietary Maillard products: iron and zinc absorption and retention$^6$</td>
<td>8/83–5/84 M</td>
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<td>26.1 ± 6.1 (20.0–39.0)</td>
<td>73.4 ± 13.5 (51.4–91.4)</td>
<td>175.4 ± 5.6 (165.2–186.6)</td>
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<td>10. Folic acid supplements: zinc and iron absorption (20)</td>
<td>1/84–7/84 M</td>
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<td>29.1 ± 5.3 (19.0–36.0)</td>
<td>85.9 ± 22.1 (64.8–134.7)</td>
<td>180.6 ± 10.3 (161.7–193.6)</td>
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<td>11. Copper and sucrose interactions$^6$</td>
<td>5/84–12/84 M</td>
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<td>26.6 ± 4.5 (21.0–32.0)</td>
<td>70.8 ± 3.4 (67.3–75.8)</td>
<td>180.8 ± 7.1 (170.1–189.9)</td>
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<td>12. Intrinsically and extrinsically labeled meat, liver, and peanut and sunflower butters: $^{65}$Cu absorption (21)</td>
<td>1/85–7/85</td>
<td>F</td>
<td>57.6 ± 5.3 (49.0–66.0)</td>
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<td>13. Marginal zinc intakes: ethanol metabolism (22)</td>
<td>1/85–7/85</td>
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<td>60.3 ± 2.5 (58.0–63.0)</td>
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<td>14. Ascorbic acid and copper intakes: indicators of copper nutriture (23)</td>
<td>7/85–6/86</td>
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<td>25.1 ± 3.5 (20.0–29.0)</td>
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<td>15. Short-term and long-term variability of nutritional status indexes (24)</td>
<td>7/85–12/85</td>
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<td>163.0 ± 5.2 (154.6–168.5)</td>
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<td>16. Aluminum, boron, and magnesium intakes: boron, calcium, and magnesium absorption and retention (25)</td>
<td>6/86–12/86</td>
<td>F</td>
<td>58.3 ± 10.2 (39.0–81.0)</td>
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<td>17. Calcium and manganese intakes: menstrual cycle symptoms (26)</td>
<td>7/87–12/87</td>
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<td>26.9 ± 6.5 (19.0–41.0)</td>
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<td>18. Boron and magnesium intakes: central nervous system activity (27)</td>
<td>1/88–7/88</td>
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<td>61.9 ± 8.2 (49.0–77.0)</td>
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<td>19. Magnesium intakes: magnesium status indicators (28)</td>
<td>7/89–12/89</td>
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<td>21. Oxidant stress by dietary factors: copper status indicators (30)</td>
<td>1/91–8/91</td>
<td>M</td>
<td>162.9 ± 6.3 (155.0–176.5)</td>
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<td>22. Meat consumption: zinc absorption and iron status (31)</td>
<td>7/92–12/92</td>
<td>F</td>
<td>62.5 ± 6.2 (51.0–70.0)</td>
<td>62.5 ± 6.2 (51.0–70.0)</td>
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<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td>68.3</td>
<td>68.3</td>
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<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
<td>159.7</td>
<td>159.7</td>
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<tr>
<td>Height (cm)</td>
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<td>159.7</td>
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</tbody>
</table>
data from the weight loss experiments collected only during the initial maintenance dietary periods.

**Magnesium supplementation**

In most of the studies (studies 1-16, 20, and 24), the basal diet was considered magnesium replete and not supplemented with magnesium. In the remainder of the studies, the basal diet was supplemented with magnesium as magnesium gluconate (except for one) as needed to meet the magnesium recommended dietary allowance (study 17: 57 mg Mg/d; study 21: 171 mg Mg/d; study 23: 114 mg Mg/d) or a specific experimental dietary magnesium value (study 16: 200 mg Mg/d; study 18: 200 mg Mg/d; study 19: 200 mg Mg/d; study 25: 207 mg Mg/d; study 26: 206 or 284 mg Mg/d; study 27: 100 or 200 mg Mg/d). For study 22, a magnesium supplement of 50 mg/d was provided as magnesium citrate dibasic.

**Magnesium balance method**

**Dietary analysis**

Balance data from the last 6–14 d of each dietary period of each study were analyzed. A duplicate diet for each subject in studies 1-14 and one representative duplicate diet supplying 8.4 MJ (2000 kcal) for all subjects in studies 14-27 were prepared daily for analysis. For all studies, the daily duplicate diets were blended, and aliquots (6% of total weight) of the daily meals were mixed well and made into 6- or 7-d composites before freezing. Aliquots of all prescribed dietary supplements, discretionary foods, and transient medications were measured for mineral content, and the mineral contributions were included as part of the dietary magnesium intake.

**Urinary and fecal analyses**

Total urine was collected by polypropylene funnels into 4-L polypropylene containers (6 mL of 6N HCl as “Baker Technical” grade added to prevent bacterial growth; JT Baker Inc, Phillipsburg, NJ). Fecal output, excluding remains left on toilet paper, was collected directly in plastic bags throughout each study with precautions to avoid trace mineral contamination. All excreta were cooled immediately after collection in a double-doored refrigerator that provided discreet sample transfer to technical staff. The last 6- or 7-d urine composites of each dietary period of each study were analyzed. A duplicate diet for each subject in studies 1-14 and one representative duplicate diet supplying 8.4 MJ (2000 kcal) for all subjects in studies 14-27 were prepared daily for analysis.

### TABLE 1 (Continued)

<table>
<thead>
<tr>
<th>Study no., study design, and reference</th>
<th>Study period</th>
<th>Sex</th>
<th>All subjects</th>
<th>Qualified subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>23. Copper intakes: copper status indicators (32)</td>
<td>1/93–7/93 F</td>
<td>Age (y)</td>
<td>62.5 ± 7.4 (49.0–75.0)</td>
<td>63.3 ± 7.2 (49.0–75.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.2 ± 10.4 (45.6–83.1)</td>
<td>68.1 ± 10.3 (45.6–83.1)</td>
<td></td>
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</tr>
<tr>
<td>Height (cm)</td>
<td>158.2 ± 6.1 (148.5–166.9)</td>
<td>158.9 ± 5.8 (148.5–166.9)</td>
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<td>n</td>
<td>13</td>
<td>12</td>
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<tr>
<td>24. Weight loss: regional body composition&lt;sup&gt;7&lt;/sup&gt; (33)</td>
<td>1/94–6/94 F</td>
<td>Age (y)</td>
<td>29.6 ± 4.2 (25.0–38.0)</td>
<td>28.3 ± 3.4 (25.0–33.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>100.3 ± 16.9 (78.0–132.5)</td>
<td>102.8 ± 21.9 (78.4–132.5)</td>
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<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167.8 ± 6.4 (159.3–182.5)</td>
<td>170.5 ± 8.0 (160.2–182.5)</td>
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<tr>
<td>n</td>
<td>12</td>
<td>6</td>
<td></td>
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<tr>
<td>25. Fructose and magnesium intakes: macromineral homeostasis (34)</td>
<td>7/94–12/94 M</td>
<td>Age (y)</td>
<td>30.4 ± 5.5 (22.0–40.0)</td>
<td>30.4 ± 5.5 (22.0–40.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.9 ± 13.1 (53.4–94.8)</td>
<td>78.9 ± 13.1 (53.4–94.8)</td>
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</tr>
<tr>
<td>Height (cm)</td>
<td>178.2 ± 9.0 (164.0–199.0)</td>
<td>178.2 ± 9.0 (164.0–199.0)</td>
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<tr>
<td>n</td>
<td>14</td>
<td>14</td>
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<tr>
<td>26. Magnesium and copper intakes: magnesium status indicators (35)</td>
<td>1/95–12/95 F</td>
<td>Age (y)</td>
<td>63.8 ± 8.6 (47.0–78.0)</td>
<td>66.9 ± 6.9 (50.0–74.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.4 ± 11.5 (50.1–89.9)</td>
<td>63.7 ± 11.3 (50.1–82.1)</td>
<td></td>
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</tr>
<tr>
<td>Height (cm)</td>
<td>160.1 ± 6.0 (149.2–176.0)</td>
<td>159.9 ± 6.8 (149.4–176.0)</td>
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<tr>
<td>n</td>
<td>25</td>
<td>13</td>
<td></td>
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<tr>
<td>27. Magnesium intakes: neuronal function&lt;sup&gt;6&lt;/sup&gt;</td>
<td>1/00–6/00, 1/01–6/01 F</td>
<td>Age (y)</td>
<td>59.6 ± 7.2 (49.0–70.0)</td>
<td>59.6 ± 7.2 (49.0–70.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.8 ± 14.5 (53.5–112.6)</td>
<td>74.8 ± 14.5 (53.5–112.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.3 ± 8.3 (151.0–180.0)</td>
<td>164.3 ± 8.3 (151.0–180.0)</td>
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<tr>
<td>n</td>
<td>14</td>
<td>14</td>
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</table>

<sup>1</sup> Metabolic studies done at the US Department of Agriculture, Agricultural Research Service, Grand Forks Human Nutrition Research Center, Grand Forks, ND, between 1976 and 2001 that measured individual dietary magnesium intake and fecal and urine magnesium output.

<sup>2</sup> For the study design, the experimental variable or variables are given, and the primary outcome measure or measures follow the colon. The reference number is in parentheses.

<sup>3</sup> Data from a specific dietary period for a person were excluded when intakes of calcium, copper, iron, phosphorus, or zinc fell below the respective estimated average requirements or exceeded the respective 99th percentiles of usual intakes from the 1994 Continuing Survey of Food Intakes by Individuals (for iron, above the upper limit) (1, 36) to avoid confounding the results with concurrent nutritional stress. To maximize consistency in data across persons, balance periods <6 d or > 12 d in length were eliminated. To meet the design criteria suggested by the Food and Nutrition Board (1), the minimum acceptable dietary adaptation period was 12 d.

<sup>4</sup> SD; range in parentheses (all such values).

<sup>5</sup> Height data were not available.

<sup>6</sup> Publication was not available.

<sup>7</sup> Study used data from maintenance diets only.
for each volunteer were prepared by combining proportional aliquots of daily urines and freezing them until analysis. Weighed fecal specimens were frozen, lyophilized, and then combined in toto in a plastic bag to prepare 6- or 7-d composites and were subsequently pulverized by a rolling pin and mixed by hand shaking for each volunteer.

Exercise

For all studies, all subjects were required to exercise a minimum of 15 min at 50% maximum work capacity on an ergocycle 3 times each week. Additional exercise was prescribed as needed to maintain body weight within 2% of initial weight. Voluntary walking regimens did not affect mandatory exercise prescriptions.

Confidentiality considerations

For each original study, a password secure, confidential computer file maintained the linkage between subject name and identification number, with access limited to select center staff members. This linkage was separate from research data files and was kept for several reasons: to provide subjects with individual study numbers, to provide governmental and institutional auditors with access as required by law. For the present study, the linkage between preexisting data files and subject was broken by the following method. The database for the original studies consisted of multiple data files, each keyed by using a unique individual identification number. A separate file was created that consisted only of records with current identification numbers along with new, randomly generated identification numbers. Subsequently, the relevant data files in the preexisting database were copied into a new database; as the file was copied, the original identification number was replaced by the randomly generated identification number. Subject names and birth dates were not copied to the new database. After the new database was created, the file containing the existing identification numbers and the randomly generated identification numbers were deleted permanently. No hard copy of this file was ever generated. In summary, all linkage was broken between the preexisting data and the original identification numbers with no possibility to associate any original data with a specific subject.

Magnesium balance calculation

Whole-body surface losses of magnesium for young men were determined (unpublished data, 1989) in one of the metabolic studies (38). Each subject showered, then put on a cotton suit of long underwear and a protective covering over briefs and socks, all provided by the metabolic unit. After 48 h, the suits were removed, and the subjects stood in a plastic tub and shower with warmed deionized water. Shaving or application of any skin care product other than the wasp soap provided by staff members was not allowed for 4 d before or during the sweat test. Whole-body surface losses of magnesium were negligible (4.1 mg/d).

The last balance periods (≤2) were selected from each available dietary period to provide 1–9 observations per subject. Magnesium balance was calculated by differences between dietary intake and fecal and urinary losses. Magnesium balance was calculated by the following equation (40):

\[ Y_{ij} = \alpha + \beta X_{ij} + a_i + b_i X_{ij} + e_{ij} \]  

where \( Y_{ij} \) is the \( j \)th magnesium output measurement on the \( i \)th subject, \( X_{ij} \) is the \( j \)th magnesium intake measurement on the \( i \)th subject, \( i = 1, \ldots, 243 \) subjects, \( j = 1, \ldots, n_i \) values, and

\[
\begin{pmatrix}
    a_i^* \\
    b_i
\end{pmatrix}
\sim iid N\left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \Sigma \right),
\]

\[
\Sigma = \begin{pmatrix}
    \sigma_a^2 & \sigma_{ab} \\
    \sigma_{ab} & \sigma_b^2
\end{pmatrix}
\] and \( e_{ij} \sim iid N(0, \sigma_e^2) \)  

Data management and statistical analysis

Confidentiality considerations

For each original study, a password secure, confidential computer file maintained the linkage between subject name and identification number, with access limited to select center staff members. This linkage was separate from research data files and was kept for several reasons: to provide subjects with individual study results and to provide governmental and institutional auditors with access as required by law. For the present study, the linkage between preexisting data files and subject was broken by the following method. The database for the original studies consisted of multiple data files, each keyed by using a unique individual identification number. A separate file was created that consisted only of records with current identification numbers along with new, randomly generated identification numbers. Subsequently, the relevant data files in the preexisting database were copied into a new database; as the file was copied, the original identification number was replaced by the randomly generated identification number. Subject names and birth dates were not copied to the new database. After the new database was created, the file containing the existing identification numbers and the randomly generated identification numbers were deleted permanently. No hard copy of this file was ever generated. In summary, all linkage was broken between the preexisting data and the original identification numbers with no possibility to associate any original data with a specific subject.
Fixed coefficients were added to the models to allow for separate intercepts and slopes for men and women to determine whether sex differences existed in the requirement estimates. The model used was as follows:

$$Y_{ij} = \alpha + \beta_1 X_{ij} + \beta_2 G_i + \beta_3 X_{ij} G_i + a'_i + b'_i X_{ij} + e_{ij}$$

(3)

where $G_i$ is 1 if subject $i$ was male or 0 if subject $i$ was female. To test whether there was an age effect on magnesium requirements, age was added to the model as follows:

$$Y_{ij} = \alpha + \beta_1 X_{ij} + \beta_2 A_i + \beta_3 X_{ij} A_i + \beta_4 X_{ij} G_i + a'_i + b'_i X_{ij} + e_{ij}$$

(4)

where $A_i$ is the age of subject $i$. The men in this study had a relatively narrow age range compared with the women. Therefore, models that included age as a predictor were also tested by using data only from women to assess whether the results obtained were simply artifacts of the different age distributions.

The 95% CIs (41) and 95% prediction intervals (PIs) (42, 43) were calculated and graphed for the final models. The magnesium requirement was defined as the point where magnesium intake given magnesium output) and calculating the PIs by using methods for random coefficient models (43).

RESULTS

A total of 664 observations from 243 subjects (women, $n = 150$; men, $n = 93$) were available for statistical analysis. Daily intakes of magnesium ranged between 84 and 598 mg. To facilitate application of the findings to the general population, the data were examined by the 3 statistical models.

Magnesium intake compared with output: statistical model A

Magnesium output ($Y$) increased linearly with increases in magnesium intake ($M$) when intake was expressed as mg/d ($P = 0.0001$) (Figure 1). Magnesium intake equaled magnesium output (crossed line of unity; neutral balance) at 165 mg/d ($Y = 19.8 + 0.880 M$; 95% PI: 113, 237 mg/d). The relation between magnesium output and intake, expressed in mg/d, was not sex dependent ($P = 0.52$). Adjusting for magnesium intake, age did not affect magnesium output ($P = 0.14$).

Magnesium intake compared with output: statistical model B

Magnesium output increased linearly with increases in magnesium intake expressed as mg · kg body wt$^{-1} · d^{-1}$ ($P = 0.0001$) (Figure 2). Accordingly, magnesium intake equaled magnesium output at 2.36 mg · kg body wt$^{-1} · d^{-1}$ ($Y = 0.306 + 0.870 M$; 95% PI: 1.58, 3.38 mg · kg body wt$^{-1} · d^{-1}$). Sex did not affect the relation between magnesium intake and output ($P = 0.23$) when the relation was expressed as mg · kg body wt$^{-1} · d^{-1}$. Adjusting for magnesium intake, the effect of age was not statistically significant ($P = 0.17$) when the relation was expressed as mg · kg body wt$^{-1} · d^{-1}$.

Magnesium intake compared with output: statistical model C

Magnesium output increased linearly with increases in magnesium intake ($Y$) when both were expressed as mg · kcal$^{-1} · d^{-1}$ (Figure 3). Across all subjects, magnesium intake equaled magnesium output at 0.075 mg · kcal$^{-1} · d^{-1}$ ($Y = 0.011 + 0.857 M$; 95% PI: 0.05, 0.11 mg · kcal$^{-1} · d^{-1}$).
relation between magnesium output and intake did not depend on
sex (P = 0.18) when expressed as mg · kcal⁻¹ · d⁻¹. Adjusting for
magnesium intake, the effect of age did not affect the relation
between magnesium intake and output (P = 0.17) when the
relation was expressed as mg · kcal⁻¹ · d⁻¹.

Magnesium balance (mg/d) compared with age

Most male and female subjects were aged 19–40 y and 50–75
y, respectively (Figure 4). To explore further the possible effects
of age, magnesium balance was modeled by using age as the
predictor. No significant relation between balance and age (in
mg/d) (P = 0.9) was indicated.

**DISCUSSION**

This study expands the magnesium balance data needed to
generate better estimates of the adult magnesium requirement.
As outlined by the FNB (1), the number of magnesium balance
studies that meet minimum design criteria is insufficient. This
study exploited the metabolic data collected from studies in
which only healthy volunteers participated, adequate dietary ad-
aptation (44) was assured by examining only dietary periods
> 27 d, magnesium intakes below and near the presumed re-
quired amounts were included, the mineral content of the drink-
ing water was measured, foods and beverages were prepared by
professional staff members for delivery within 1% weighing
error, duplicate diets were prepared by professional staff mem-
bers, food consumption was quantitative and carried out under
visual supervision, fecal and urine collections were continuous to
ensure familiarity with the procedure, and samples were ana-
lyzed by state-of-the-art technology. Excluding data when in-
takes of measured minerals fell below the EARs eliminated the
possibility of confounding the data set with potential catabolic
states that result in release of magnesium from tissues (44).

**Magnesium homeostasis**

Characteristics of the statistical models indicate strong ho-
meostatic control of magnesium metabolism. The regression
lines crossed respective lines of unity at highly acute angles, a
characteristic that indicates magnesium balance is highly resis-
tant to change across a broad range of typical dietary magnesium
intakes. The homeostatic mechanisms seemed particularly active
below neutral magnesium balance. Within the range of dietary
magnesium intakes examined, the data did not reach an asym-
tote, indicating no change in magnesium fractional intestinal
absorption over the typical range of dietary magnesium intakes.

**Estimations of the average magnesium requirement**

The statistical models used in the present study predict neutral
magnesium balance at magnesium intakes of 165 mg/d for
healthy persons regardless of age or sex. Therefore, compared
with the existing EAR, the new estimate of the magnesium re-
quirement is 35–48% lower for women and 50–53% lower for
men. The diets and environments used by the metabolic studies
were a reasonable approximation of the free-living environment.
For example, the amount and type (swimming, walking, station-
ary biking) exercise was prescribed per individual and therefore
varied considerably among subjects.

An EAR includes an adjustment for an assumed bioavailabil-
ity of the relevant nutrient (1). Therefore, the findings from
the present study may have particular relevance to the general pop-
ulation because most of the magnesium intake values examined
were generated from studies in which the diets were not supple-
mented with magnesium. Equally important, all diets were com-
posed of ordinary Western foods and constructed in such a man-
ner as to ensure a high degree of compositional heterogeneity
across meals and studies.

Some magnesium intake values used in the present study were
based on diets composed of ordinary Western foods and supple-
mented with magnesium (all data points in studies 17 and 21–23,
and ~50% of all data points from studies 16, 18, 19, and 25–27).
For all those studies except study 22, the supplemental magnesium was supplied as magnesium gluconate. If the bioavailability of magnesium in magnesium gluconate is greater than that of dietary magnesium, inclusion of such data should artificially reduce the estimated magnesium requirement. However, findings from the relevant metabolic studies indicate that providing supplemental magnesium as magnesium gluconate did not improve magnesium absorption. Instead, this form of supplementation reduced the percentage of magnesium intake excreted in the urine (25, 27).

**Comparative magnesium balance studies**

Magnesium balance was considered the only reliable indicator of magnesium status when setting the current adult magnesium EARs (1). The FNB examined 9 magnesium balance studies (7, 9–11, 45–49) and excluded 2 because of inadequate assessment of dietary magnesium near the predicted requirement (11) or insufficient adaptation periods (45).

For adult women of all ages, the magnesium EARs are based nearly exclusively on the findings from one study (7) of adults (aged 20-53 y; 16 men; 18 women) who consumed self-selected diets in a free-living environment. Subjects were responsible for collection and transport of food and excreta, and magnesium intakes decreased substantially when subjects were fed a high-fiber, low-protein diet (46). For men, estimations of the magnesium requirement rely heavily on results from the primary study used to establish the EAR for women (7). Magnesium intakes decreased substantially during the balance period, and mean magnesium balance was negative. A different metabolic study (49) with 5 men diagnosed during the balance period, and mean magnesium balance was found to be 0 mg/d (2). In the present study, diets supplied between 12 mg/d and 10 mg Mg/d were sufficient to maintain balance close to equilibrium but were not as close when fed a high-fiber, low-protein diet (46).

For men, estimations of the magnesium requirement rely heavily on results from the primary study used to establish the EAR for women (7). Magnesium intakes decreased substantially during the balance period, and mean magnesium balance was negative. A different metabolic study (49) with 5 men diagnosed with either psychoneurosis or osteoporosis showed that a magnesium intake of 240 mg/d was sufficient to maintain balance close to equilibrium but were not as close when fed a high-fiber, low-protein diet (46).

For men, estimations of the magnesium requirement rely heavily on results from the primary study used to establish the EAR for women (7). Magnesium intakes decreased substantially during the balance period, and mean magnesium balance was negative. A different metabolic study (49) with 5 men diagnosed with either psychoneurosis or osteoporosis showed that a magnesium intake of 240 mg/d was sufficient to maintain balance close to equilibrium but were not as close when fed a high-fiber, low-protein diet (46).

For all those studies except study 22, the supplemental magnesium was supplied as magnesium gluconate. If the bioavailability of magnesium in magnesium gluconate is greater than that of dietary magnesium, inclusion of such data should artificially reduce the estimated magnesium requirement. However, findings from the relevant metabolic studies indicate that providing supplemental magnesium as magnesium gluconate did not improve magnesium absorption. Instead, this form of supplementation reduced the percentage of magnesium intake excreted in the urine (25, 27).

**Magnesium balance and age or sex**

Age did not affect the relation between magnesium intake and output, similar to the findings of an earlier study (7). A separate study (5) found no association with age on urinary magnesium excretion (fetal magnesium excretion not measured), when expressed per millimole of creatinine. The effect of age on body stores of magnesium in healthy older adults was examined previously (50, 51). An observed increase in percentage retention of an intravenous magnesium load test in older adults (50) may have been confounded by the severe unequal distribution of men and women in the experimental group such that the findings may relate more to sex or body size differences than to age. A separate study reported a decrease in erythrocyte magnesium in the older adults compared with younger adults (51), but findings on erythrocyte magnesium content were not considered sufficiently predictive to be of use in establishing an EAR (1).

Findings that the relation between magnesium intake and output is not affected by sex concur with earlier findings of balance from a study with subjects on self-selected diets (7). In a separate study, sex did not affect urinary magnesium excretion after corrections were made for body size (5).

In summary, findings from the present study augment the sparse information available for calculating the EAR for magnesium. They suggest a lower magnesium requirement for healthy men and women than estimated previously.

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CDH was responsible for the conception of the experimental design, data selection, data analysis, and the writing of the manuscript. LKJ was responsible for data selection, data analysis, and statistical modeling procedures and was involved in the preparation of the article. None of the authors had any financial or personal conflict of interest.

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