Nutrition and Optimizing Development of Peak Bone Mass

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Half of women over age 50 will have a fracture.

World wide cost of hip fracture - $131 billion

Maximizing Bone Mineral Content Reduces Risk of Fracture

Calcium storage in bone is a functional reserve

http://www.ohsuhealth.com/dch/health/orthopaedics
Peak Bone Mass Starts in Utero

Atkinson SA. McMaster University 2005
Bone Mass Throughout Life Influenced by Calcium Intake

Adequate Calcium Intake With Exercise During Teenage Years May Help Reduce Risk for Osteoporosis

- Adequate Calcium Intake
- Inadequate Calcium Intake
- Fracture Zone
Why it is so difficult to determine the role of nutrition in health?

• The process of chronic disease is long
  
  *and grant periods are short*

• Observational research does not establish cause and effect

• Ultimate disease outcomes not often relevant in children and biomarkers are often lacking
Setting Calcium Requirements
Dietary Reference Intakes

- EAR (Estimated Average Requirement)
- RDA (Recommended Dietary Allowance)
- UL (Tolerable Upper Intake Level)

Risk of inadequacy

Risk of excess

Intake

0.5

- Risk of inadequacy
- Risk of excess
Range of mean intakes from 20 countries

mg/day

Percent of adolescents and adults in 20 countries meeting country-specific Ca recommendations

Bars represent highest and lowest values and black box indicates range of 75% of range

Calcium

No status indicator and estimates of dietary intake are fraught with error

Underreporting error for energy intake in overweight boys and girls was 35±18%

Singh, AJCN 89:2009

Singh, AJCN 89:1744, 2009
Improving Dietary Assessment Methods Using the Mobile Phone and Digital Imaging

• Develop a tool for recording dietary intake
  • Use a mobile phone with digital camera--2-d pictures
  • Image processing to identify food in real time
    • Supplement with label from search list
    • Calculate volume to estimate portion size
• Software calculates nutrient intake
To achieve a range in known calcium intakes in various populations, metabolic balance studies have been used by most countries. We don’t have the data to use RCTs for setting Ca requirements.
Effect of Ca supplementation on upper limb BMD in children

<table>
<thead>
<tr>
<th>Study</th>
<th>N (Treatment)</th>
<th>Mean (SD)</th>
<th>N (Control)</th>
<th>Mean (SD)</th>
<th>SMD (fixed) (95% CI)</th>
<th>Weight (%)</th>
<th>SMD (fixed) (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Johnston 1992</td>
<td>45</td>
<td>317.09 (69.40)</td>
<td>45</td>
<td>311.51 (69.67)</td>
<td>5.81 0.08 (-0.33 to 0.49)</td>
<td>10.22</td>
<td>0.17 (-0.15 to 0.46)</td>
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<tr>
<td>Lee 1994</td>
<td>77</td>
<td>487.00 (41.00)</td>
<td>82</td>
<td>480.00 (43.00)</td>
<td>10.22 0.17 (-0.15 to 0.46)</td>
<td>6.96</td>
<td>0.14 (-0.24 to 0.51)</td>
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<td>Bonjour 1995</td>
<td>55</td>
<td>312.00 (29.66)</td>
<td>53</td>
<td>308.00 (29.12)</td>
<td>5.41 0.02 (-0.41 to 0.45)</td>
<td>5.41</td>
<td>0.02 (-0.41 to 0.45)</td>
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<td>Lee 1995</td>
<td>44</td>
<td>492.00 (39.00)</td>
<td>40</td>
<td>491.00 (51.00)</td>
<td>10.40 0.20 (-0.10 to 0.51)</td>
<td>10.09</td>
<td>0.44 (0.12 to 0.75)</td>
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<td>Wang 1996</td>
<td>79</td>
<td>486.00 (37.00)</td>
<td>83</td>
<td>479.00 (31.00)</td>
<td>10.09 0.44 (0.12 to 0.75)</td>
<td>10.09</td>
<td>0.44 (0.12 to 0.75)</td>
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<td>Dibba 2000</td>
<td>80</td>
<td>253.00 (50.00)</td>
<td>80</td>
<td>231.00 (50.00)</td>
<td>8.41 0.22 (-0.12 to 0.56)</td>
<td>3.10</td>
<td>0.09 (-0.47 to 0.66)</td>
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<tr>
<td>Stear 2003</td>
<td>65</td>
<td>427.00 (38.00)</td>
<td>66</td>
<td>418.00 (43.00)</td>
<td>3.10 0.09 (-0.47 to 0.66)</td>
<td>11.22</td>
<td>0.23 (-0.06 to 0.53)</td>
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<tr>
<td>Cameron 2004</td>
<td>24</td>
<td>418.00 (43.00)</td>
<td>24</td>
<td>414.00 (42.00)</td>
<td>14.97 0.05 (-0.21 to 0.30)</td>
<td>4.19</td>
<td>-0.23 (-0.72 to 0.26)</td>
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<td>Matkovic 2004</td>
<td>79</td>
<td>450.00 (53.00)</td>
<td>96</td>
<td>438.00 (50.00)</td>
<td>9.23 -0.05 (-0.38 to 0.27)</td>
<td>100.00</td>
<td>0.14 (0.04 to 0.24)</td>
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<tr>
<td>Chevalley 2005</td>
<td>114</td>
<td>309.60 (28.00)</td>
<td>118</td>
<td>308.20 (32.00)</td>
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<td>Courteix 2005</td>
<td>22</td>
<td>336.18 (43.19)</td>
<td>63</td>
<td>351.00 (69.75)</td>
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<td>Prentice 2005</td>
<td>73</td>
<td>479.00 (61.00)</td>
<td>70</td>
<td>482.00 (51.00)</td>
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<td></td>
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<tr>
<td>Total (all data)</td>
<td>757</td>
<td></td>
<td>822</td>
<td></td>
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</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2 = 8.69$, df=11, $P=0.65$, $I^2=0$
Test for overall effect: $z=2.71$, $P=0.007$

Winzenberg et al BMJ 2006
Most country requirements are based on balance studies.
FAO/WHO

Relationship between calcium absorption and calcium intake

Ch. 11 Calcium  FAO/WHO expert consultation on human vitamin and mineral requirements, pp 151-179
Calcium intakes required to provide the absorbed calcium necessary to meet calcium requirements at different stages in the lifecycle.

Note: The solid lines represent the mean and range of calcium absorption as a function of calcium intake derived from the equation in Figure 14. The interrupted lines represent the estimated calcium requirements based on Western European and North American data.
North America

Calcium Intake for Maximal Retention at 3 Life Stages
Adolescence: Period of Rapid Bone Accretion

Camp Calcium
Metabolic Studies in Adolescents
How much Calcium?

Funded by NIH (NIAMS)
Camp Calcium Studies

• 10 metabolic balance studies, 1990 to 2007
• Adolescent boys and girls
• **Controlled** diets for 3 week metabolic balance periods
• Urine and fecal collections pooled by 24h
• Calcium retention (mg/d) =
  \[ \text{Ca intake (mg/d)} - \text{Urinary Ca}^* (mg/d) - \text{Fecal Ca} (mg/d) \]

*creatinine-corrected
Camp Calcium  June 1999
Study Design

Controlled diet *High* or *Low* Ca or Salt

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Controlled diet *High* or *Low* Ca or Salt

Crossover

Washout

Metabolic Balance

Metabolic Balance
Maximal Calcium Retention as a Function of Intake

% Maximum Retention

Intake (mg/day)

Over 1 year, represents gain of 4% skeleton

Jackman et al., AJCN, 1997
Boys have higher bone accretion than girls

Bailey, et al., JBMR 14:711, 1999
Camp Calcium tested whether boys require more calcium for their larger skeletons

Boys matched for Tanner Stage to girls ~3.6

Braun et al., AJCN, 84:4142006
Calcium retention was greater in white boys compared to white girls but the intake for maximal retention was not different from girls (1140 mg/d vs 1300 mg/d).

Boys retain 171 ± 38 mg more calcium than girls at all intakes.

Braun et al., AJCN, 84:4142006
Some have questioned the relevance of balance studies to reflect long term skeleton growth
Pubertal White Boys

Calcium intake for maximal retention by balance = 1140 mg/d

Mean Maximal Ca retention = 442 mg/d

Longitudinal total body BMC accrual on Ca intakes = 1140 ± 392 mg/d

Mean Ca retention = 359 mg/d

Hill et al. JCEM 93:4743, 2008
Pubertal White Girls

Balance: Mean Ca retention on Ca intake of 1113 mg/d = 238 mg/d

Longitudinal total body BMC accrual: Mean Ca retention on Ca intakes of = 1113 ± 378 mg/d = 284 mg/d

Hill et al. JCEM 93:4743, 2008
Role of Race?
Differences in Regulators of Calcium Metabolism

Whites have higher Ca intake and Vitamin D status, but lower PTH than other groups.
Diet and race effects on Ca retention in adolescent girls

Ca Intake explained 12.3% and Race explained 13.7% Ca retention in adolescent girls

Braun et al. AJCN 85:1657-63, 2007

Camp Calcium
Bone formation

Bone resorption

Intestine

Vi

intake

absorption

Va

Vf

fecal

Ca Pool

Kidney

Vf

Vf

Vf

Vf

Vo-

Vo+

Vu

urine

Vf

Vf

Vf

Vf

Vf

Vf

Vf
Blacks compared to whites

Calcium Retention as a function of postmenarcheal age in black and white females

Blacks 12% onset + 20 yrs

In NHANES III,

Femoral neck BMC and BMD was 10% and 13% higher, respectively, in adult black than white women.
Difference in Bone accretion between Chinese and White girls

Chinese American Camp Calcium 2005

- 16 healthy Asian boys and 15 healthy Asian girls aged 11-14 y from IL, IN, and MI.

Converted residence hall into metabolic ward
Asian Camp Calcium Study Design

Compliance
• Urinary Cr
• Fecal PEG recovery =81.3%

Controlled diet
High or Low Ca

Week
1 2 3 1 2 3

Crossover
Washout

Ca isotopes
Metabolic Balance

Ca isotopes
Metabolic Balance
Calculated Intake for Maximal Retention in Chinese American Boys

*=1110 mg/day

Compared to 1140 mg/d for white boys
Calcium Intake for Maximal Retention in Chinese American Girls

*=970 mg/day

Compared to 1300 mg/d for white girls
Racial Differences in Calcium Absorption with Intake

![Graph showing the relationship between calcium intake (mg/d) and % of ⁴⁴Ca dose/L, categorized by race (Asian girls, White girls, Black girls). The graph demonstrates a proportional decrease in % Ca absorption with increasing calcium intake.]
Race differences in calcium absorption and retention explain much of black/white differences in bone, but not Asians.

Very low calcium intakes explain smaller Asian BMC.

Yao Ming 7’6”- he must drink milk.
Role of Salt
Effect of dietary salt in calcium retention

• Metabolic balance study
  - Randomized order
  high/low salt

• Adolescent black and white subjects matched for size and sexual maturity

Dietary salt varied

Low Na diet $\rightarrow$ 1.3 g/d
High Na diet $\rightarrow$ 4 g/d
Urinary sodium excretion (Mean±SEM)

Low Na diet (1.3 g/d)  High Na diet (4 g/d)

* Significantly different from whites at p<0.05

Urinary calcium excretion
(Mean ± SEM)

Calcium retention
(Mean ± SEM)

Ca Retention (mg/d)

Low Na diet (1.3g/d)  High Na diet (4 g/d)

* p<0.05 for diet and race
Candidate genes for racial differences in response to salt relate to Na/Ca transporters

ENAC

Explanation for racial differences in incidence of hypertension and osteoporosis
Fractures Also Occur in Young

Trends in fracture incidence from Khosla et al. JAMA 2003;290:1470

Figure from Heaney and Weaver JACN 2005;24:574
Risk taking or low bone density?
Transient Low BMD for Size

Size-adjusted BMD

BMD = bone mineral density (g/cm²)

Faulkner et al., J Bone Miner Res 2006;21:1864
Higher Fracture Incidence Coincides with Low BMD for Size

(Radial fractures are total # over 14 years)

Faulkner et al., J Bone Miner Res 2006;21:1864
Increased rate of fracture in adolescence is a result of the sequence of normal growth events…

(...But…)
Incidence of Distal Forearm Fractures in Adolescents has Increased

Khosla et al., JAMA 2003;290:1470
Dietary calcium mainly comes from dairy
Children who avoid milk are at ↑Risk for bone fracture!

Milk avoider’s

Fracture Risk 34.8%
Birth cohort 13.0%

Goulding et al. JADA 104:250,2004
Bone healthy diet

Calcium rich foods, dairy
Fruits/Vegetables
Whole grains

Benefits of Diet:
Maximize peak bone mass
Minimize bone loss
Promote overall health
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