Linear Growth Retardation (Stunting) and Nutrition

Ricardo Uauy
INTA University of Chile and London School of Hygiene and Tropical Medicine
Stunting prevalence and number affected in developing countries

Source: Department of Nutrition, World Health Organization
171 million children under 5 are stunted

Source: WHO Global Database on Child Growth and Malnutrition, May 2009
Stunting

Most common form of undernutrition (PE/micronutrients)

Affects infants before and early after birth

Linked to maternal size, nutrition during pregnancy & fetal growth

Length that is lost early on is rarely recovered

Stunted have less lean body mass (lower RMR per kg bw)
Methods

• Data from WHO Global Database on Child Growth and Malnutrition - standardized data

• National surveys from 54 countries (52 DHS and 2 MICS) - all but 7 surveys conducted since 2000

• 32 low income, 17 lower middle income, 5 upper middle income

• Re-analyzed raw datasets with WHO standards - calculated mean WAZ, HAZ, WLZ by month

• Countries aggregated by WHO regions - only 2 countries in WPRO, grouped with EURO (Mongolia) and SEARO (Cambodia)

Mean $z$-scores for age all 54 studies, relative to the WHO standard

Family Diet and Health in Pre-War Britain

A DIETARY AND CLINICAL SURVEY

Carnegie United Kingdom Trust
COMELY PARK HOUSE, DUNFERMLINE, FIFE
SCOTLAND
1955
Milk/ Animal source foods interventions improve linear growth

1930s  UK: Boyd Orr: feeding trials of surplus milk disposal to school children: significant increase in height, improvement in “general appearance”.

India: Aykroyd and Krishnan (1937) skimmed milk supplemented school children grew faster in height


US: Fomon et al. (1977): skimmed milk (low energy, high protein)-fed infants showed same length growth but less weight gain than high energy formula.

Bangladesh: Kabir et al (1992/3): ASF protein at 15% energy increases IGF-1 and linear growth cf 7.5% protein in children recovering from shigellosis
Overall and cause specific mortality hazard ratios (95% CI) for men and women in relation to 1 SD increase in overall height and leg length adjusted for childhood socioeconomic deprivation, calorie consumption, birth order, and adult Townsend score

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>No of deaths</th>
<th>Height</th>
<th>Leg length</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men (n=1129)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All causes</td>
<td>207</td>
<td>1.06 (0.92,1.24)</td>
<td>0.97 (0.82,1.15)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>106</td>
<td>0.85 (0.69,1.06)</td>
<td><strong>0.79 (0.62,1.00)</strong></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>77</td>
<td>0.84 (0.65,1.08)</td>
<td>0.79 (0.60,1.04)</td>
</tr>
<tr>
<td>Non-cardiovascular, smoking related</td>
<td>38</td>
<td><strong>1.49 (1.06,2.11)</strong></td>
<td>1.33 (0.88,2.01)</td>
</tr>
<tr>
<td>Cancer</td>
<td>51</td>
<td><strong>1.42 (1.05,1.91)</strong></td>
<td>1.38 (0.98,1.96)</td>
</tr>
<tr>
<td>Non-smoking related cancer</td>
<td>20</td>
<td>1.30 (0.80,2.11)</td>
<td>1.44 (0.83,2.49)</td>
</tr>
<tr>
<td>Other causes</td>
<td>49</td>
<td>1.20 (0.87,1.64)</td>
<td>1.03 (0.73,1.47)</td>
</tr>
<tr>
<td><strong>Women (n=1195)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All causes</td>
<td>148</td>
<td>0.92 (0.77,1.11)</td>
<td>0.97 (0.80,1.17)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>50</td>
<td>0.81 (0.59,1.10)</td>
<td><strong>0.72 (0.52,1.00)</strong></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>26</td>
<td><strong>0.56 (0.36,0.88)</strong></td>
<td><strong>0.52 (0.33,0.83)</strong></td>
</tr>
<tr>
<td>Non-cardiovascular, smoking related</td>
<td>28</td>
<td>1.08 (0.71,1.66)</td>
<td>1.15 (0.73,1.79)</td>
</tr>
<tr>
<td>Cancer</td>
<td>60</td>
<td>0.98 (0.74,1.32)</td>
<td>1.04 (0.77,1.41)</td>
</tr>
<tr>
<td>Non-smoking related cancer</td>
<td>39</td>
<td>0.99 (0.69,1.42)</td>
<td>1.07 (0.74,1.54)</td>
</tr>
<tr>
<td>Other causes</td>
<td>38</td>
<td>1.00 (0.69,1.44)</td>
<td>1.25 (0.85,1.83)</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01.
Infection and other Environmental Factors

Nutrition

Fetal & Infant nutrition

Diet

Growth muscle/bone
Weight & HEIGHT
Body composition

Brain Development

Metabolic Programming
CHO, Lipids, Proteins
hormone, receptor, gene

Short term

Cognitive capacity & Education

Immunity
Work Capacity

Long term

Diabetes
Obesity
Cardiovascular Disease,
Stroke Hypertension
Cancer
Aging

Infection and other Environmental Factors

Genes
Nutrient Effects on Growth

• Any essential nutrient can condition abnormal embryonic & organ growth and development (Folate, I, Vit A, E, Fe, Zn, EFA, EAA Pr/Energy)

• Timing of nutrient deficit or excess is crucial in effect: cell replication/migration/apoptosis/maturation

• Genetic polymorphism affecting nutrient metabolism transport or tissue levels can modulate effects.

• Nutrients & toxicants (retinoic acid, Pb, Zn, folate) interact in defining normal or abnormal growth.
Nutrient/Hormones Effects on Growth

**Hyperplasia**
- Insulin, IGF1/ BP3
- Cortisol
- Leptin, GH
- T3/ T4

**Brain**
- I, Fe, Cu, Zn,
- Na, K, P,
- Energy
- n-6 & n-3 EFA

**Bone / length**
- Aminoacids

**Hypertrophy**

**Adipose tissue/ weight**
Mechanisms by which nutrition conditions linear growth

- Gene Expression (transcription factors, single or multiple genes)

- Hormones receptors, binding proteins and signal transduction

- Cell growth and turnover during critical periods
**Nutrition: protein & zinc**

**IGF-1, IGF-BPs, T3**

**Infection:** Inhibits chondrogenesis
Cortisol, IL1, TNF, IL6, increase bone destruction

**Oestrogens main regulator of pubertal growth spurt & GP fusion**

**Linear Growth**
- Resting cell layer
- Proliferating chondrocyte layer
- Layer of maturing and enlarging chondrocytes
- Layer of dying and calcifying chondrocytes
- Osteoblast activity
Nutrition and infection influence bone length growth

**Nutrition Type 2 nutrients:** protein & zinc

**Chondrogenesis & chondrocyte maturation:**
- IGF-1, IGF-1BPs, T3
- TGFβs (transforming growth factor)
- BMPs, (bone morphogenetic proteins)
- Oestrogens main regulator of pubertal growth spurt and GP fusion

**Infection:** Inhibition of chondrogenesis
- Cortisol, IL1, TNF, IL6, increase bone destruction

**Growth hormone**
- Increase in insulin-like growth factor 1

**Osteoclasts**

**Circulating osteoblasts**

**Osteogenic cells in bone marrow**

**Systemic circulation**

**Endochondral bone formation**

**Periosteum**

**Osteoblast**

**Osteoclast**

**T3**

**chondrocytes**
Kofoed et al. describe a novel mechanism for impaired growth in the form of a mutation in the gene for intra-cytoplasmic protein signal transducer and activation of transcription 5b (STAT5b).

The mutation disrupts the intracellular signalling that promulgates the physiologic effects of growth hormone. This finding illuminates an important arena of molecular genetic abnormalities involving the growth hormone–insulin-like growth factor I (IGF-I) axis.

GH activated signalling. Phosphorylation of the GH receptor leads to activation of metabolic, proliferative and transcriptional pathways. STAT 5b modulates transcription of IGF-1, IGF-BP3, and acid labile subunit, all critical for normal growth.
Maternal protein flux and neonatal length

Length of the newborn at birth and maternal protein synthesis in mid pregnancy for 26 women

Sarah L. DUGGLEBY* and Alan A. JACKSON
Linear growth (cm/week)
Kashyap 1988 and Svenningsen 1982 found no significant difference in linear growth between groups. These findings differed from Kashyap 1986’s study that noted a significant increase in linear growth in infants receiving higher protein intakes.

The inclusion of the Kashyap 1988 study in the meta-analysis revealed a significant difference (WMD 0.16 cm/week, 95% 0.03, 0.30), with greater linear growth with high protein intakes compared to low protein intakes.

**LBW protein intake and length growth**

- Study participants were less than 2.5 kilograms at birth
- Study participants were not receiving parenteral nutrition at time of randomization
- Study participants were exclusively formula-fed
- Energy, Na, K, P, Zn or essential fatty acid intakes did not differ significantly (no more than 10% relative concentration)
<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>N</th>
<th>Mean (SD)</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Mean Difference IV, Fixed, 95% CI</th>
<th>Weight</th>
<th>Mean Difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1 Weight gain (g/kg/day)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bhatia 1991</td>
<td>16</td>
<td>20.3 (2.31)</td>
<td>7</td>
<td>18.9 (1.2)</td>
<td>1.40 [ -0.04, 2.84 ]</td>
<td>52.7 %</td>
<td></td>
</tr>
<tr>
<td>Hillman 1994</td>
<td>18</td>
<td>17.4 (3.6)</td>
<td>9</td>
<td>12.9 (5.3)</td>
<td>4.50 [ 0.66, 8.34 ]</td>
<td>7.4 %</td>
<td></td>
</tr>
<tr>
<td>Kashyp 1986</td>
<td>9</td>
<td>18.3 (2.8)</td>
<td>9</td>
<td>13.9 (2.8)</td>
<td>4.40 [ 1.81, 6.99 ]</td>
<td>16.3 %</td>
<td></td>
</tr>
<tr>
<td>Svenningsen 1982</td>
<td>16</td>
<td>13.8 (4.1)</td>
<td>14</td>
<td>13.3 (3.9)</td>
<td>0.50 [ -2.37, 3.37 ]</td>
<td>13.3 %</td>
<td></td>
</tr>
<tr>
<td>Wauben 1995</td>
<td>8</td>
<td>16.45 (3.51)</td>
<td>8</td>
<td>11.54 (3.15)</td>
<td>4.91 [ 1.64, 8.18 ]</td>
<td>10.2 %</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>67</td>
<td></td>
<td>47</td>
<td></td>
<td></td>
<td>100.0 %</td>
<td>2.36 [ 1.31, 3.40 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 9.25, df = 4 (P = 0.06); I² = 57%
Test for overall effect: Z = 4.42 (P < 0.00001)

| **2 Linear growth (cm/week)** | | | | | | | |
| Kashyp 1986      | 9  | 1.21 (0.32) | 9  | 0.94 (0.19) | 0.27 [ 0.03, 0.51 ] | 53.6 % | | |
| Svenningsen 1982 | 16 | 1.02 (0.38) | 14 | 0.99 (0.35) | 0.03 [ -0.23, 0.29 ] | 46.4 % | | |
| **Subtotal (95% CI)** | 25 | | 23 | | | 100.0 % | 0.16 [ -0.02, 0.34 ] |

Heterogeneity: Chi² = 1.74, df = 1 (P = 0.19); I² = 42%
Test for overall effect: Z = 1.75 (P = 0.081)

| **3 Head growth (cm/week)** | | | | | | | |
| Kashyp 1986      | 9  | 1.22 (0.28) | 9  | 0.85 (0.15) | 0.37 [ 0.16, 0.58 ] | 100.0 % | | |
| **Subtotal (95% CI)** | 9  | | 9  | | | 100.0 % | 0.37 [ 0.16, 0.58 ] |

Heterogeneity: not applicable
Test for overall effect: Z = 3.49 (P = 0.00048)
Test for subgroup differences: Chi² = 17.70, df = 2 (P = 0.00), I² = 89%
VLBW Calorie and protein intake on IGF-1

Smith, W. J. et al. J Clin Endocrinol Metab 1997;82:3982-3988
VLBW Calorie and protein intake on IGFBP-3

Smith, W. J. et al. J Clin Endocrinol Metab 1997;82:3982-3988
Dexamethasone .25/mg x 2 x 7 days affects Linear Growth and Neurodevelopment

- Cerebral palsy: 17/72 vs. 9/74
- Intelligence Q: 78.2 vs. 84.4
- Manual dexterity: 6.6 vs. 4.8
- Balance: 6.9 vs. 3.2
- Total impairment: 19 vs. 11
- Motor coordination: 6.7 vs. 8.2
- Visual perception: 6.5 vs. 7.9
- Visual–motor int: 7.1 vs. 7.9

Tsu F Yeh et al NEJ Med 2004
Abstract. Growth and nutrition data from the feasibility phase of a clinical trial that was designed to evaluate the effect of diet protein modification in 24 infants with chronic renal insufficiency (CRI). GFRs less than 55 ml/min per 1.73 m².

Twenty-four infants were randomly assigned at 8 mo of age to receive a low-protein (P : E ratio 5.6%) or control protein (P: E ratio 10.4%) formula, average intakes of 1.4 and 2.4 g/kg/d in low & control groups.

Length/age Z at entry (low -2.2 ± 1.4 vs. control -1.7 ± 1.4). At 18 months the low protein group had a significantly lower length Z (-2.6± 1.2 vs. while control remained unchanged -1.7± 1.4).

The length velocity Z from 12 to 18 months were also different, with the low-protein group remaining strongly negative while the control group improved.
Energy and Protein intakes in the lower and higher protein groups

(n=540) low-protein 1.8-2.2 g/100Kcal
(n=550) high-protein 2.9-4.4 g/100Kcal
(n=588) breastfed children

Higher protein intake increases weight for length \( (n=540) \) low-protein 1.8-2.2 g/100Kcal \( (n=550) \) high-protein 2.9-4.4 g/100Kcal \( (n=588) \) breastfed children

Protein content for first yr of life

\( (n=540) \) low-protein 1.8-2.2 g/100Kcal
\( (n=550) \) high-protein 2.9-4.4 g/100Kcal
\( (n=588) \) breastfed children

Mean z scores (95% CI)

\*P < 0.05 \**P < 0.01 \***P < 0.001
Significantly different from the Low Protein group (ANOVA adjusted for baseline value)

Anthropometry During Recovery from PEM

% of Standard

Weight for Age
Length for age
Weight for length

Months of treatment

0 1 2 3 4 5
Protein & energy needs for catch-up growth at varying rate of weight gain

<table>
<thead>
<tr>
<th>Rate of gain g/kg/d</th>
<th>Protein e (g/kg/d)</th>
<th>Energy f (kcal/kg/d)</th>
<th>Protein/Energy (%)</th>
<th>Protein g (g/kg/d)</th>
<th>Energy h (kcal/kg/d)</th>
<th>Protein/Energy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.02</td>
<td>89</td>
<td>4.6</td>
<td>1.0</td>
<td>91</td>
<td>4.2</td>
</tr>
<tr>
<td>2</td>
<td>1.22</td>
<td>93</td>
<td>5.2</td>
<td>1.1</td>
<td>97</td>
<td>4.5</td>
</tr>
<tr>
<td>5</td>
<td>1.82</td>
<td>105</td>
<td>6.9</td>
<td>1.5</td>
<td>115</td>
<td>5.2</td>
</tr>
<tr>
<td>10</td>
<td>2.82</td>
<td>126</td>
<td>8.9</td>
<td>2.2</td>
<td>145</td>
<td>6.0</td>
</tr>
<tr>
<td>20</td>
<td>4.82</td>
<td>167</td>
<td>11.5</td>
<td>3.6</td>
<td>205</td>
<td>6.9</td>
</tr>
</tbody>
</table>

a: 73-27% lean:fat equivalent to 14% protein and 27% fat   b: 50:50% lean :fat equivalent to 9.6% protein and 50% fat
c: based on 5.65kcal/g protein and 9.25kcal/g fat
d: net costs adjusted for a 90% and 73% metabolic efficiency of fat and protein deposition respectively plus ME of additional non-utilized protein
e: 14% deposited tissue adjusted for a 70% efficiency of utilization plus the safe level of maintenance at 1.24*0.66g/kg/d =0.82(see text)
f: maintenance energy at 85kcal/g, (which includes maintenance protein energy) + gross energy costs at 4.10kcal/g weight gain.
g: 9.7% deposited tissue adjusted for a 70% efficiency of utilization plus the safe level of maintenance at 1.24*0.66g/kg/d=0.82g/kg/d 1.27*.58 g/kg/d =0.737
h: as in f except that gross energy costs are 5.99kcal/g weight gain.

FAO/WHO 2008 TRS 935
WHICH NUTRIENTS CAN PROMOTE LINEAR GROWTH?
### Type I and type II nutrients and the characteristics of their deficiency

**See:** Severe malnutrition: *Hum Nutr. & Dietetics* 10th Ed M. H. N. Golden B. E. Golden

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue level</td>
<td>variable</td>
<td>fixed</td>
</tr>
<tr>
<td>Used in specific pathways</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Characteristic physical signs</strong></td>
<td></td>
<td><strong>No characteristic signs</strong></td>
</tr>
<tr>
<td><strong>Late or no growth response</strong></td>
<td></td>
<td><strong>Immediate growth response</strong></td>
</tr>
<tr>
<td>Stored in body</td>
<td></td>
<td>No body store</td>
</tr>
<tr>
<td>Buffered response</td>
<td></td>
<td>Responds to daily input</td>
</tr>
<tr>
<td>Not interdependent</td>
<td></td>
<td>Control each others' balance</td>
</tr>
<tr>
<td>Little excretory control</td>
<td></td>
<td>Sensitive physiological control</td>
</tr>
<tr>
<td><strong>Unlikely to influence length growth</strong></td>
<td></td>
<td><strong>Likely to influence length growth</strong> (in most cases)</td>
</tr>
</tbody>
</table>

### Nutrients

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodine</td>
<td>Ascorbic acid</td>
<td>Nitrogen</td>
</tr>
<tr>
<td>Iron</td>
<td>Retinol</td>
<td>Essential amino acids</td>
</tr>
<tr>
<td>Copper</td>
<td>Tocopherol</td>
<td>Potassium</td>
</tr>
<tr>
<td>Calcium</td>
<td>Calciferol</td>
<td>Sodium</td>
</tr>
<tr>
<td>Manganese</td>
<td>Folic acid</td>
<td>Magnesium</td>
</tr>
<tr>
<td>Selenium</td>
<td>Cobalamine</td>
<td>Zinc</td>
</tr>
<tr>
<td>Thiamin</td>
<td>Pyridoxine</td>
<td>Phosphorus</td>
</tr>
<tr>
<td>Riboflavin</td>
<td></td>
<td>Water</td>
</tr>
</tbody>
</table>
Nutrition and height growth: specific nutrients

**Protein**
- strong experimental evidence in animals
- Good indirect data in humans

**Zinc**
- Good experimental evidence in animals
- Good meta analysis data in humans (weak effect)

**Calcium & Phosphate**
- Length growth not thought to be limited by mineral supply in general

**Other micronutrients:**
- I, Fe, Mn, Ca, vitamin A, Vit D all potentially involved but specific deficiency signs & symptoms would be observed.

**Infection/stress:**
- Good experimental and epidemiological evidence mediated by pro inflammatory cytokines & cortisol
Epidemiology: Milk/Animal source foods improve height growth

**Uganda:** Rutishauser and Whitehead (1969): faster height growth of Karamoja children, (milk and meat), compared with Bugandan children (plantains).

**Peru:** Graham et al. (1981): attained height of boys strongly associated with protein intake.

**Korea:** Paik et al. (1992), height-for-age correlated with animal protein intake in Korean school children.

**Denmark:** 2004 IGF-I & height positively associated with milk intake not meat or vegetable protein at 2.5 years: milk increases IGF-1 in 8-year-old Danish boys.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>0.59</td>
<td>0.05</td>
</tr>
<tr>
<td>Pregnancy fat gain</td>
<td>0.23</td>
<td>0.000</td>
</tr>
<tr>
<td>Lactation weight gain</td>
<td>0.24</td>
<td>0.02</td>
</tr>
<tr>
<td>Child supplementation</td>
<td>-0.19</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Neumann et al 1994
<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length at 18 mo</td>
<td>0.87</td>
<td>0.000</td>
</tr>
<tr>
<td>Maternal fat intake</td>
<td>0.17</td>
<td>0.001</td>
</tr>
<tr>
<td>Season</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>Household size</td>
<td>-0.08</td>
<td>0.072</td>
</tr>
</tbody>
</table>

Neumann et al 1994
<table>
<thead>
<tr>
<th></th>
<th>Regression coefficients</th>
<th>p&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Length velocity of children (18-30mo)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R^2$ 0.27  n=118</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal fat intake</td>
<td>0.25</td>
<td>0.018</td>
</tr>
<tr>
<td>Season</td>
<td>0.27</td>
<td>0.005</td>
</tr>
<tr>
<td>Household size</td>
<td>-0.14</td>
<td>0.12</td>
</tr>
<tr>
<td>Child’s fat intake</td>
<td>0.38</td>
<td>0.025</td>
</tr>
<tr>
<td>Iron intake</td>
<td>0.45</td>
<td>0.07</td>
</tr>
<tr>
<td>Diarrhea (% days)</td>
<td>-0.18</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Neumann et al 1994
Meat diet boosts kids' growth

Bringing up children as vegans is unethical argues Lindsay Allen of the University of California, Davis, who carried out the research.

2-year study of Kenyan 7y olds, given 60g minced beef/d
Children showed improved B12 status
- up to an 80% greater increase in upper-arm muscle
- outperformed their peers in intelligence, problem solving and arithmetic
- were more active in the playground, more talkative and playful, and showed more leadership skills,

USAID: Global Livestock CRSP Child Nutrition Program (Kenya study)

2-yr study of Kenyan 7y olds Design: daily snacks 1000–1125 kJ at school (5 per wk)
1) Control: no snack
2) Energy snack: Veg stew: maize, beans and vegetables + fat
3) Milk snack: Veg stew plus 200 mL milk
4) Meat snack: Veg stew + 60 g minced beef.

Trial confounded by changes in food intake at home. Only meat snack group increased energy intake.

Effects of meat

↑ MUAC
↑ Cognitive Development
↑ Plasma B12
No influence on height growth
New Guinea children grow taller with skim milk

- Children were stunted but otherwise OK on their low protein diets
- Height growth increased with skim milk

- **Protein intake (g/kg):** Control 0.64, Margarined 0.63, Taro 1.13, Milk 2.24
- **Energy intake (Kcal/kg):** Control 59.5, Margarined 100, Taro 152, Milk 107
- **P:E %:** Control 4.3, Margarined 2.5, Taro 3.2, Milk 8.4

Meat/milk eating African children are taller/thinner than those eating mainly starchy foods.

Karamoja (herdsman: milk/meat) Tall/normal height: thin
Buganda (farmers: plantains) Short and fat

Child growth is slightly impaired on vegan diets:

In preschool children who are vegan with slower growth, lack of meat and all other ASF, maintaining energy density can be problematic. After this stage of life, growth of vegan children in the USA and UK differs only very slightly from the reference populations (e.g. -0.1 SD for height at 10 years).


(from Millward & Garnet Proc Nutr Soc (2010), 69, 103–118)
**Zinc: Animal studies**

Zinc stimulates bone protein synthesis and bone formation


**Human foetal growth**

RCT of prenatal zinc supplementation and foetal bone growth

Impoverished Peruvian women: daily supplements of 60mg Fe and 250µg folic acid, +/- 25 mg Zn

Femur diaphysis length greater in foetuses of zinc supplemented mothers ($P<0.05$)

Effect size of Zn on Height mean 95% CI

Brown K et al AJCN 2002
RAT STUDIES:- PROTEIN AND ENERGY
Mechanisms and interrelationships of action on bone and muscle growth in the rat

probed by measurements of:

- bone growth: tibial length and epiphyseal cartilage width
- muscle growth: gastrocnemius muscle growth
- protein synthesis: $^{14}$C-phe large dose
- proteoglycan synthesis: $^{35}$S uptake
- insulin, T3 and plasma and tissue IGF-1

Protein specifically regulates bone length growth:

**Graph 1:**
- **tibial length growth (mm/d)**
- **days of diet**
- **dietary protein**
  - • 20% age control
  - ◆ 20%
  - ○ 7%
  - ▲ 3.5%
  - □ 0.5%

**Graph 2:**
- **tibial length growth (mm/d)**
- **days of refeeding**
- **dietary protein**
  - • 20% age control
  - ◆ 20%
  - ○ 12%
  - ▲ 9%
  - □ 6%
  - △ 3%
Protein deficiency is as powerful as energy deficiency \textit{if not more so}, in inhibiting tibial length growth.

- **Dietary protein concentration**
  - 20%
  - 7%
  - 3.5%
  - 0.5%

- **Dietary energy at iso N Intake**
  - 100%
  - 50%
  - 75%
  - 25%
  - CS*

* corticosterone: to give plasma levels observed after prolonged starvation
Long bone growth and protein and energy deficiency: summary of findings

- Epiphyseal cartilage width, protein and proteoglycan synthesis inhibited within 3 days of protein deficiency
- Actual length growth inhibition observed after 3 days of protein deficiency
- Dietary protein can maintain bone growth in conditions of modest energy deficiency which reduces bodyweight
- Insulin, T3 and IGF-1 all fall with protein deficiency, but relationships with changes in proteoglycan synthesis and epiphyseal cartilage are not symmetrical.
- Corticosteroids mediate main inhibitory influence of severe energy deficiency, possibly also in acute malnutrition
Linear Growth and body composition are controlled mainly at the level of long bone growth and muscle growth.

**Bone Growth**
- Bone length growth is the primary driver of whole body linear growth.
- Genetic determination of rate/time course (canalization).
- Dietary protein and other type II nutrients are key regulators: Protein more powerful than energy in the rat.

**Skeletal Muscle Growth**
- Growth rate and target weight controlled by bone length growth.
- Passive stretch: physiological stimulus for growth.
- Target weight requires adequate dietary protein.
- Muscle activity required for maximum phenotypic muscle mass.

**Body Growth**
- Growth driven by functional demand and food intake.
- Protein Energy.

Serial length measurements of normal infants were assessed weekly, semiweekly or daily 19 females/12 males during their first 21 mo
What is Optimal Growth

• Paradigm of “bigger is better” has never been tested critically, are we really promoting “heavier is better”?

• NCHS-WHO standards reflect feeding practices of USA community where reference data was obtained, population has significant burden of chronic disease

• New WHO standards for weight and length are based on NEW feeding recommendations, leaner and taller

• “Normal” standards should be validated relative to early and late measures of health. Optimal should be based on lowest morbidity and healthy lifespan.
Probability of Obesity in Boys according to Height

Length Z Score age 6 yrs

- 1987-90
- 1993-96
- 2000-02
Pre Pregnancy BMI

Maternal Glucose Insulin

Placental Fetal blood flow

Hormonal responses

Fetal growth restriction

Fetal Macrosomia

Hormonal responses

Energy Balance

Pubertal Sexual maturation

Early Adiposity rebound

feeding fast Weight gain

Central Obesity Metabolic syn

High BMI Obesity