Acid Base Balance and Skeletal Health

- Acid precursors: sulfur containing amino acids in all proteins
- Base precursors: alkaline potassium salts in fruit/vegetables (Kcitrate, KHCO₃)
- Does exposure to a net dietary acid load mobilize base from bone to titrate dietary acid?
Long-term Potential Effects of a Net Dietary Acid Load

- Skeleton
  - Physiochemical effect
  - Cell mediated
- Muscle
  - ↓ IGF-1
  - Mobilization of glutamine
- Effects of age-related decline in renal function
- ? Net effect = bone / muscle loss

Relationship is Complex

- Primary focus on protein (acid)
- Protein only half the equation: hunter-gatherer diets
  - ~250 g/d protein
  - typically net base producing
- Hunter-gatherer diet = 88 meq/day base
- Western diet = 58 meq/day acid

**Sulfur-containing AA (g) per 10g Protein**

- spaghetti noodles
- haddock
- white rice
- chicken
- english muffin
- ground beef
- cottage cheese
- milk
- soybeans
- Grt North beans
- peanut butter
- peas
- almonds

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**Improving Dietary Acid-Base Balance**

- **Option 1: Less acid**
  - Reduce dietary protein, cereal grains
  - Protein important for peak bone mass, skeletal maintenance, healing

- **Option 2: More base**
  - Dietary (potassium-rich fruit / veggies)
  - Alkaline potassium supplements
    - Potassium bicarbonate
    - Potassium citrate
Alkaline K Salts and Ca Metabolism

• ↓ Urine calcium excretion
• Calcium balance = dietary calcium intake –
  (urine calcium + fecal calcium)
  – n=10, KHCO₃⁻ 60 mmol/d x 12 days
  • Ca balance = + 36 mg/day
  – n=18, KHCO₃⁻ 60-120 mmol/day x 18 days
  • Ca balance = + 56 mg/day
  – Intestinal absorption not directly measured


Alkaline K Salts and Ca Metabolism

• Intestinal fractional calcium absorption
  (oral / IV stable isotopes)
  – n=18, KCitrate 40 mmol/d x 14 days
  • No effect on fractional calcium absorption
  – x-sectional, n=191, free living diet
  • Potassium intake inversely
    associated with calcium absorption
  • Potassium from milk / meat
    rather than fruit / veggies

Calcium Absorption and Balance
6 Month Intervention

Change in urine calcium excretion (mg/day)
Change in fractional calcium absorption (%)
Change in calcium balance (mg/day)

Placebo
K Citrate 60 mmol/day
K Citrate 90 mmol/day

*p<0.05 compared to placebo

Markers of Bone Turnover

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>K Citrate 60 mmol/day</th>
<th>K Citrate 90 mmol/day</th>
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</thead>
<tbody>
<tr>
<td>BsAP (μg/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11.8 ± 1.3</td>
<td>11.8 ± 1.3</td>
<td>11.3 ± 1.1</td>
</tr>
<tr>
<td>Change</td>
<td>-0.95 ± 0.8</td>
<td>-1.1 ± 0.9</td>
<td>-1.8 ± 0.8</td>
</tr>
<tr>
<td>Serum CTX (ng/ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.19 ± 0.04</td>
<td>0.25 ± 0.03</td>
<td>0.25 ± 0.04</td>
</tr>
<tr>
<td>Change</td>
<td>0.04 ± 0.03</td>
<td>-0.07 ± 0.04</td>
<td>-0.03 ± 0.04</td>
</tr>
</tbody>
</table>

*p<0.05 vs. placebo

**KCitrate and BMD**


161 postmenopausal women
30 mmol/day

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<th>3 Months</th>
<th>6 Months</th>
<th>9 Months</th>
<th>12 Months</th>
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<tbody>
<tr>
<td>Lumbar Spine</td>
<td>+ 1%</td>
<td>0%</td>
<td>-1%</td>
<td>-2%</td>
</tr>
<tr>
<td>Total Hip</td>
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**KCl vs KCitrate**


276 postmenopausal women
KCitrate 55.5 mmol/d, 18.5 mmol/d, fruit / veggies, placebo
No effect BMD, urine calcium
N=201
60% female
25(OH)vit D = 24 ± 8 ng/ml
L Spine T-score = -0.6 ± 1.5

Kcitrate 60 mmol/day vs. pbo
NAE negative on Kcitrate
↑ trabecular thickness, number on QCT.

Kcitrate and BMD

Isoflavones/Soy

• Plant compounds (phytoestrogens) found in soybeans, clover, alfalfa sprouts
• Studies on bone health mixed
  – Interventions varied
  – Different compounds may offset each other
  – Effects may depend on proximity to menopause
  – Equol producers
  – 2 placebo controlled RCTs neg
**Sodium Chloride**

- ↑ dietary NaCl ↑ urine calcium, bone resorption
- Effects on fracture not known
- Dietary K and base (fruit and vegetables) offset NaCl effects
- High salt foods:
  - prepared foods--jars, cans, boxes, bottles
  - condiments, sauces
  - cheese, bread
  - restaurants
- Current RDA: 1500mg/day; AHA rec: 2400mg/day

**Phosphorus**

**Relationship to Skeleton**
- Essential for bone building and growth
- 85% of body’s P bound to skeleton

**The Issues**
- Excess PO4 → ↑ PTH → ? bone resorption
- Typical intakes > RDA (700 mg/day)
- PO4 intake ↑’ing due to preservatives
- High dietary Ca ↓ absorption dietary PO4

**Sources**
- Meat, poultry, fish, eggs, dairy, nuts, legumes, cereals, grains, cola

**Bottom Line**
- Typical intakes (1000-1500 mg/day) prob OK unless dietary Ca low
- Poor overall nutrition = low PO4 intake
- ? Important during anabolic osteoporosis tx
Magnesium

Relationship to Skeleton
- Essential for bone formation
- 2/3 of body’s Mg in skeleton (surface)
- Impt for proper crystal formation during mineralization

The Issues
- Deficiency → impairs PTH secretion → hypocalcemia, vitamin D resistance
- Typical intakes < RDA
- RDA 320 mg women, 420 mg men, +35 mg preg

Sources
- Whole grains, green vegetables, squash, nuts, seeds, “hard” water

Bottom Line
- Typical intakes appear low
- EtOH → Mg wasting
- Effect on skeletal health not clear

Iron

Relationship to Skeleton
- Co-factor for enzymes involved in collagen synthesis

The Issues
- ↓ bone strength Fe deficient rats
- Fe absorption decreased by other minerals esp Ca
- Fe overload states associated with ↓ trabecular volume, number, thickness

Sources
- Dark green veg, spinach, red meat

Bottom Line
- Separate Fe and calcium supplements
- Unclear how much of bone deficits in overload states due to Fe itself
**Zinc**

**Relationship to Skeleton**
- Co-factor for enzymes involved in collagen synthesis and mineralization

**The Issues**
- ↓ bone formation in Zn deficient rats
- Low Zn levels associated with osteoporosis in humans
- Zn supplements improved BMD in rats

**Sources**
- Red meat, poultry, fish, oysters, eggs, legumes, whole grain breads, milk

**Bottom Line**
- Zn stimulates osteoblasts, bone formation in animal studies
- EtOH → Zn wasting
- Need human intervention studies

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**Copper**

**Relationship to Skeleton**
- Involved in collagen maturation, cross linking

**The Issues**
- Typical intakes < RDA
- Cu deficiency assoc with ↓ osteoblast function
- Trace mineral supplement incl Cu increased BMD

**Sources**
- Legumes, nuts, mushrooms, liver, oysters, cereals, chocolate

**Bottom Line**
- Need human intervention studies
**Vitamin A and Carotenoids**

**Relationship to Skeleton**
- Vitamin A involved in bone remodeling process
- Animal foods: retinol; vegetables: carotenoids

**The Issues**
- Excess and deficiency Vit A ↑ skeletal fragility
  - ↑ intakes/↑ serum retinol levels associated with ↓ BMD, ↑ fracture in some human studies
  - β-carotene, lycopene, leutein assoc with ↑ BMD, ↓ bone loss, ↓ hip fracture

**Sources**
- red/orange/yellow vegetables (β-carotene), dark green veg (lutein), tomatoes, watermelon (lycopene), liver, dairy products, fish

**Bottom Line**
- Avoid excess or insufficient Vit A intake (3000 IU per day in supplements)
- Vegetable sources also provide antioxidants

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**Vitamin B12**

**Relationship to Skeleton**
- May effect osteoblast function/activity

**The Issues**
- Low serum B12 associated with ↓ BMD, ↑ bone loss, ↑ fracture in most human studies
  - Supplementation with B12 and folate in CVA population ↓ hip fracture risk (RCT)

**Sources**
- Fish, shellfish, meat, poultry, eggs, milk

**Bottom Line**
- Be alert to states associated with ↓ B12
  - Vegan
  - Pernicious anemia
  - Gastric bypass
  - Atrophic gastritis (up to 40% elderly)
  - Celiac, Crohn’s, other GI disease
**Vitamin C**

**Relationship to Skeleton**
- Required for collagen crosslinking

**The Issues**
- Deficiency state (scurvy)—defective collagen matrix, ↑ bone resorption, osteoporosis, fractures
- ↓ serum levels common in elderly, institutionalized
- Smoking ↓ intestinal absorption, increases catabolism
- ↑ Vit C intake associated with ↑ BMD, ↓ bone loss, ↓ fractures

**Sources**
- Fresh fruits and vegetables

**Bottom Line**
- Low with tobacco, EtOH
- Malabsorptive states
- Ensure fresh fruit/veg intake in at risk individuals

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**Vitamin K**

**Relationship to Skeleton**
- Co-enzyme for carboxylase enzyme
- Carboxylated osteocalcin attracts Ca, enhances mineralization

**The Issues**
- Undercarboxylated osteocalcin associated with ↑ bone resorption, fracture
- Low serum Vit K assoc with lower BMD, ↑ fracture risk
- Intervention studies mixed: BMD neg, fx +

**Sources**
- K1: Broccoli, cabbage, spinach, brussel sprouts, turnip greens, lettuce, vegetable oils; K2: meat, eggs, dairy, natto (ferm soy)
- Many veg's good sources both Vit K and Ca
- May be issue in malabsorption, chronic antibiotic use
- 2 Viactiv chews = 80 mcg (DRI ~90-120 mcg)
- MK4 used as osteoporosis therapy in Japan
Summary

• No fracture data; minimal BMD data

• Protein
  – Ensure adequate protein intake (0.8 g/kg/day)
  – Soy/isoflavones
    • great vegetarian protein source
    • great calcium source
    • interest diminishing for isoflavones for bone

• Robust intake of fruit/vegetables (4 cups women, 5 cups men)

• Limit sodium chloride

• Be aware of particular conditions associated with deficiencies/excesses of trace minerals, vitamins

Questions?