SLAMMD

Nutrition SMO

Protein (and muscle)

Countermeasures

Dietary Protein
Unloading-induced atrophy is a relatively uncomplicated form of muscle loss. Most of the loss of muscle mass during disuse atrophy can be accounted for by a depression in the rate of protein synthesis.

whereas in disease states associated with inflammation (cancer cachexia, AIDS, burns, sepsis, and uremia), there is a procatabolic hormonal and cytokine environment. ....

Inflammation

Inflammatory Markers
It is imperative that these studies include examination of dynamic measures of muscle protein turnover and putative metabolic controllers... unless we have a clear idea of the basic responses to immobilization per se, the effects of such factors will not be easily teased out and therapeutic goals will remain largely unattainable.

Hyper-catabolism

Hyper-catabolic conditions associated with proteolysis:
- Cancer cachexia
- Cachexia associated with heart failure
- Sepsis
- Starvation
- Metabolic acidosis
- Stress/trauma associated with excess glucocorticoids
- Space flight

Omega 3 (n3) Fatty Acids

- Eicosapentaenoic acid (EPA)
  - 20-C, omega-3 fatty acid
  - Dietary sources: fish oil, flaxseed, walnuts
- Beneficial effects on cholesterol, lipid metabolism, and cardiovascular health
**Omega-3 and Cancer**

Proportion of tumor-bearing rats

Vanamala et al., Carcinogenesis, 2008

**Vitamin D**

**Sources**
- UVB radiation
- Food
  - Seafood, mushrooms, egg yolk,
  - Fortified foods

**Nomenclature**
- Vitamin D$_{2}$ (ergocalciferol)
- Vitamin D$_{3}$ (cholecalciferol)
- 25-OH vitamin D
- 1,25(OH)$_{2}$ vitamin D

**Vitamin D Intake Guidelines**

- RDA (1997 IOM)
  - 19-50 y: 200 IU/d
  - 50-70 y: 400 IU/d

The 2005 Dietary Guidelines for Americans recommendation advised older adults, people with dark skin, and people exposed to insufficient sunlight to consume 1000 IU/d.

**Contributing Factors to Vitamin D Status**

- Age
- Ethnicity
- Salt-sensitive hypertension
  - Increased protein excretion in salt-sensitive individuals and Dahl rats with salt loading
- Adiposity/obesity
Vitamin D is associated with:
- Calcium metabolism
- Fracture Risk/BMD

Smith et al., J Nutr, 2006
Smith et al., J Nutr, 2005

Vitamin D status has been related to:
- Fractures, fracture risk, BMD
- Muscle strength/function, falls
- Cancer (prostate, breast, colon)
- Multiple sclerosis
- Blood pressure/heart disease
- Diabetes (type 1)
- Multiple Sclerosis
- Dementia
- Parkinson's Disease
- Tuberculosis
- Incidence of C-section
- The common cold
- Incidence of C-section

Vitamin D and PTH
- Erkal, Osteo Int, 2006
- Thomas et al., NEJM, 1998
- Chapuy et al., Osteo Int, 1997

Vitamin D status has been related to:
- Fractures, fracture risk, BMD
- Muscle strength/function
- Cancer (prostate, breast, colon)
- Multiple sclerosis
- Blood pressure/heart disease
- Diabetes (type 1)

Bischoff-Ferrari, Am J Clin Nutr, 2006

Recommendations
- Encourage adequate vitamin D:
  - Intake
    - Fortified milk, orange juice
    - Fish (salmon, tilapia, tuna)
    - Few other sources...
  - Sunlight
  - Supplements

...the criterion for broad-based supplementation in the general population is not fulfilled, except for in high risk groups, such as the elderly...all other persons with negligible exposure to sunshine.

Space Food

<table>
<thead>
<tr>
<th>Flight Requirement (per day)</th>
<th>VD D (IU)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>450</td>
</tr>
<tr>
<td>Salmon</td>
<td>296</td>
</tr>
<tr>
<td>Tuna</td>
<td>152</td>
</tr>
<tr>
<td>Breakfast Drink</td>
<td>118</td>
</tr>
<tr>
<td>Tuna Noodle Casserole</td>
<td>66</td>
</tr>
<tr>
<td>Cornflakes</td>
<td>68</td>
</tr>
<tr>
<td>Tuna Salad Spread</td>
<td>64</td>
</tr>
<tr>
<td>Bran Chex</td>
<td>68</td>
</tr>
<tr>
<td>Scrambled Eggs</td>
<td>64</td>
</tr>
<tr>
<td>Bread Pudding</td>
<td>53</td>
</tr>
<tr>
<td>Granola w/Raisins</td>
<td>44</td>
</tr>
<tr>
<td>Teriyaki Beef</td>
<td>36</td>
</tr>
<tr>
<td>Pork Chops</td>
<td>32</td>
</tr>
<tr>
<td>Vegetable Quiche</td>
<td>28</td>
</tr>
<tr>
<td>Pudding Soup</td>
<td>28</td>
</tr>
</tbody>
</table>
Upper Limits

2000 IU/day is current defined IOM no observed adverse events limit (NOAEL).

Studies of higher levels have proven safe...

Sunlight does not result in toxicity
Watch multivitamins (vit A and other nutrients may be in excess)

Vitamin D Toxicity

Hypercalcemia, hypercalciuria, soft tissue calcification, kidney stones

Vitamin D

Vitamin D status goes down after long-duration spaceflight.

Questions:
Is the stability of vitamin D in the food system and supplement different during spaceflight?
Is the daily dose not high enough to maintain status?
Does vitamin D metabolism change during spaceflight?

Stability Study

Stability of vitamin D in food-supplement is not altered during spaceflight

Question:
Is the daily dose simply not high enough to maintain status in an environment with no sun exposure?
3 levels of vitamin D supplementation:
- 400 IU/d (n = 18)
- 1000 IU/d (n = 19)
- 2000 IU/d (n = 18)

3 blood collections and diet logs
- 25D, 1,25D, PTH, Ca, VDBP, NTX

Double blinded supplementation (Smith et al., 2009)

Compliance
- 84% on average (Smith et al., 2009)

Vitamin D status is related to body weight…
- what if we exclude subjects with BMI >29 kg/m²?

1000 or 2000 IU/d was enough to reach 80 nmol/L and maintain vitamin D status

Residual Questions…
- Could compliance be improved with a weekly dose instead of a daily dose?
- Is vitamin D status related to observed changes in immune function during polar winters?
In addition to BMI, the efficacy of vitamin D supplementation is affected by baseline status.

Compliance:
- 2000 IU/d – 91%
- 10000 IU/wk – 97%

Residual Questions…
Is a higher, less frequent dose as effective as a daily or weekly dose?
Does a high dose result in a high serum concentration of 25-OH vitamin D (or metabolites) or alter serum or urine calcium?

Vitamin D Dosing Study
2,000 IU/d
10,000 IU/wk
50,000 IU weekly x4; then 1/mo
Vit D (and metabolites)
Ca, etc.
Dist, university
1 subject in 2000 IU/d group had 2 values >150 nmol/L.
2 subjects in 50000 IU group had 3-5 values > 150 nmol/L.

Nutrition SMO

Calcium
Collagen Crosslinks

Bone Resorption

Space Flight:

- Urinary collagen xlinks
- Urinary Ca
- Urinary OH-Proline
- Urinary N-Telopeptide

Bone resorption is increased during flight

Bone Formation/Resorption

Calcium Isotopes

$\delta^{44}Ca = \left( \frac{^{44}Ca}{^{44}Ca_{baseline}} - 1 \right) \times 1000$

Higher $\delta^{44}Ca$ = "heavier"
Lower $\delta^{44}Ca$ = "lighter"

Calcium Isotopes

<table>
<thead>
<tr>
<th>Calcium Isotopes</th>
<th>40Ca</th>
<th>42Ca</th>
<th>43Ca</th>
<th>44Ca</th>
<th>46Ca</th>
<th>48Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>97%</td>
<td>0.65%</td>
<td>0.11%</td>
<td>2.09%</td>
<td>0.004%</td>
<td>0.19%</td>
</tr>
</tbody>
</table>

Smith et al., JCEM, 1998

Smith et al., JCEM, 1998

Skulan et al., Clin Chem, 2007

Skulan et al., Clin Chem, 2007
Regenerative ECLSS

URINE PROCESSOR ASSEMBLY

Recycle Filter Tank Assembly
Distillation Assembly

URINE CALCIUM

Urine Volume

Urine Calcium

Urine Volume

+24%

-17%
Current folate intakes do not maintain folate status
How much folate is in the food? If enough – then:
Is folate stable on orbit? If it is – then:
What is changing?

Nutrient Stability

Radiation

Vitamin E
Vitamin K

**Fluid Intake**

Day 1-85
Day 131-179
Day 86-130 (Vitamin K)

Pre                Mission               Post

**UOsteocalcin (%)**

Fluid Intake
3000
4000

**Fluid Shift**

Total Body Water
ECF and Plasma Volumes
SLS-1 and SLS-2

**Renal Stone Risk**

**Nutrition SMO**

**UMS**
Excess sodium intake (and related effects on acid/base physiology) is associated with a number of health issues:

- Bone loss
- Increased renal stone risk
- Impaired muscle performance/protein catabolism
- Altered glucose metabolism
- Altered vitamin D metabolism
- Hypertension

With the exception of hypertension, all of these other factors have been raised as concerns for space travelers.
Acidosis

From Dr. L. Frassetto (UCSF) 10/6/09 JSC presentation

Pharmacologic effects of acidosis

Acid/Base and Bone

Excess dietary sodium

Na+/H+ exchange in skin GAGs

Iron (RBCs, and oxidative damage)

Iron and Oxygen

Radiation/oxygen issues have implications for cataracts and other health issues.

Total Body Iron

Radiation/oxygen issues have implications for cataracts and other health issues.

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Radiation/oxygen issues have implications for cataracts and other health issues.
Potential Countermeasures

- Nutrition
- Exercise
- Pharmacology
- Gravity

Artificial Gravity.1

Exercise Countermeasures

Bone Resorption
Dietary protein increases urinary calcium
Oxidation of excess protein yields acid (H+, H₂SO₄)
Renal buffering
Bone: reservoir of base
Osteoclasts are more active at lower pH
Excess protein: beneficial or harmful to bone?
Many factors influence the net effect

Animal protein
Diets rich in animal protein tend to have greater overall acid potential
Renal net acid excretion

Vegetables/fruits
Also contain substantial amounts of base precursors (and K)
APro/K provides an estimation of acid/alkali load
**Pro K**

**Controlled dietary intake**
- High or Low APro:K
- Monitored dietary intake

**Blood/Urine markers**

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**EXAMPLE Menu**

<table>
<thead>
<tr>
<th>High APro/K Day 1 Example</th>
<th>Low APro/K Day 1 Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oatmeal w/ Brown Sugar</td>
<td>Oatmeal w/ Raisins &amp; Spice</td>
</tr>
<tr>
<td>Soup &amp; Salad</td>
<td>Vegetarian Vegetable Soup</td>
</tr>
<tr>
<td>Grilled Chicken</td>
<td>Chicken Noodle Soup</td>
</tr>
<tr>
<td>Peanut Butter</td>
<td>Peanut Butter</td>
</tr>
<tr>
<td>Carrot Coins</td>
<td>Carrot Coins</td>
</tr>
<tr>
<td>Creamed Spinach</td>
<td>Creamed Spinach</td>
</tr>
<tr>
<td>Macadamia Nuts</td>
<td>Macadamia Nuts</td>
</tr>
<tr>
<td>Tofu</td>
<td>Tofu</td>
</tr>
<tr>
<td>Cocoa</td>
<td>Cocoa</td>
</tr>
<tr>
<td>Tofu</td>
<td>Tofu</td>
</tr>
<tr>
<td>Japanese Tomato</td>
<td>Japanese Tomato</td>
</tr>
<tr>
<td>Jelly Drink</td>
<td>Jelly Drink</td>
</tr>
<tr>
<td>Water (250 mL)</td>
<td>Water (250 mL)</td>
</tr>
<tr>
<td>Water (250 mL)</td>
<td>Water (250 mL)</td>
</tr>
</tbody>
</table>

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**Nutrition and Bone**

**Pro K**
Acid/Base and Bone

High protein, low potassium diet

Acid Load >> Alkali Load

\[ \text{H}^+ \text{ >> Organic anions} \]

\[ \text{Na}^+/\text{H}^+ \text{ exchange in skin} \]

\[ \text{GAG} \text{ - GAG} \text{ - Na}^+ \text{ excretion} \]

Excess dietary sodium

Inflammation

Bed rest
Hindlimb unloading
Spaceflight
Ionizing radiation/UVC

Arachidonic acid
PIF
LPS
RANKL
TNF-\( \alpha \)

NF-\( \kappa \)B
NF-\( \kappa \)B (active)
NF-\( \kappa \)B (inactive)

kB Inhibitor

Muscle proteolysis

Inflammatory Markers

Inflammation/Bone

MTX (nmol/d)

TNF-\( \alpha \) (pg/mL)