Nutritional Strategy

Protein breakdown

Protein synthesis

Energy and amino acids

Metabolic Regulators
HMB- ( dibutyl 
hydroxy dibutyl
methyl
butyrate)
HMB:

Theory:
- Cholesterol synthesis may limit cell growth/repair at certain times
Human Studies w/ HMB

- Adjunct for muscle building (Comparisons)
- Safety
- Combinations
- Other effects
HMB and Resistance training

Net gain lean (%/wk)

- Nissen et al. 1996
- Panton 2000
- Kreider et al. 1999
- Gallagher et al. 2000
- Slater et al. 2001
- Vukovich et al. 2001

3/29/2002
## Safety: 3-12 weeks

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>No Adverse effects</td>
</tr>
<tr>
<td></td>
<td>*Decreased BP</td>
</tr>
<tr>
<td>Blood chemistry</td>
<td>No adverse changes</td>
</tr>
<tr>
<td></td>
<td>*Lower cholesterol</td>
</tr>
<tr>
<td>Blood hematology</td>
<td>No adverse changes</td>
</tr>
<tr>
<td>Emotional</td>
<td>No adverse changes</td>
</tr>
<tr>
<td></td>
<td>*Less negative mood</td>
</tr>
</tbody>
</table>
Meta-Analysis:

- Body composition
- Minimum 3-weeks
- Minimum trained 2x per week
- Placebo controlled
- Statistical information for ES
- Protein-(placebo issues)
Meta-analysis: 250+ included

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Qualified studies</th>
<th>Quality score</th>
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<tbody>
<tr>
<td>Creatine</td>
<td>15</td>
<td>37</td>
</tr>
<tr>
<td>HMB</td>
<td>9</td>
<td>35</td>
</tr>
<tr>
<td>Chromium</td>
<td>12</td>
<td>33</td>
</tr>
<tr>
<td>Androstenedione</td>
<td>3</td>
<td>32</td>
</tr>
<tr>
<td>DHEA</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>Protein</td>
<td>4</td>
<td>27</td>
</tr>
</tbody>
</table>
Lean Tissue Gain

![Bar chart showing % gain per week for various treatments](image)
Meta-Analysis

Lean Tissue Gain

Strength Gain

Creatine HMB Chromium Androstenedione DHEA Protein

Effect Size

0.00 0.05 0.10 0.15 0.20 0.25

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HMB and Creatine

<table>
<thead>
<tr>
<th></th>
<th>HMB</th>
<th>Creatine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lean gain</strong></td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td>(weight training)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fat loss</strong></td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>(weight training)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Health benefits</strong></td>
<td>++++</td>
<td>++-</td>
</tr>
<tr>
<td>(BP and cholesterol lowered)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Runner benefit</strong></td>
<td>++</td>
<td>+++-</td>
</tr>
<tr>
<td>(protect muscle)</td>
<td></td>
<td>(risk of muscle damage)</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Minimizing Muscle damage

CPK after a 10K race

CPK change (%)

Pre Post Day 1 Day 2 Day 3 Day 4

Placebo

HMB

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HMB effects on Damage

- CPK is 30-80% lower
- Less muscle breakdown
  - Lower 3-methylhistidine
  - Lower proteases
- Less soreness

Muscle stress results in tears in cell membrane

Muscle CPK leaks into the blood
Other observations

- Less Protein turnover (muscle)
- Young and old: Men and women
- Effect proportional to intensity
- Immune function improved
Non exercising

- Sedentary young people
  - HMB: No demonstrable effect
  - Creatine: No demonstrable effect

- Wasting?
Mechanism of wasting

**Normal**

- Protein synthesis
- Protein breakdown

**Wasting**

- Protein breakdown
- Protein synthesis
Age-related muscle mass

Muscle mass

Age

<70%: Zone where Risk of Death is high

100% of max

80% of max

70% of max

25 y

50 y

75 y

<70%: Zone where Risk of Death is high

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Disease-related wasting

- Most AIDS patients waste
- Nearly all stage 2-4 lung, pancreas, colon and upper GI cancers
- >10% muscle loss = risk

Question: Can targeted nutrition reverse wasting?
Targeted Nutritional Strategy

Protein
- Break-down
- Slow
- HMB

Glutamine
- Enhance
  - Protein synthesis
  - Slow

Arginine
Elderly protocol

- Age ~78 years
- Two replicate experiments
- Mostly women
- 12 week study
- Endpoints: lean tissue/mobility
- Assisted living
- 2 g HMB/5 g Arg/ 1.5 g Lysine
- Once per day
Body Composition changes

Body lean: +1 kg

Lean change

% Change over 12 wks

Iowa

TN
Function
(Get-Up & Go)

**Placebo**
- Start
- +12 wks

**HMB/Arg/Lys**
- Start
- +12 wks

Get-Up & Go time (sec)

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AIDS/Cancer Protocols

- **AIDS**
  - Lost >5% BW
  - 36 subjects/8 wks

- **Cancer**
  - Lost 10% BW
  - 40 subjects/8+wks

- **Mixture**
  - 3 g HMB
  - 15 g Arginine
  - 15 g Glutamine
AIDS/Cancer comparison

Lean gain or loss (Kg)

2.5 **

HMB/Arg/Gln

1.4 **

Placebo

AIDS subjects

Cancer subjects

3/29/2002
HMB + amino acid

- Targeted nutritional strategy valid
- Very slight wasting can be reversed
- Very severe wasting can be reversed
- Multi-center studies underway
Muscle-Immune connection

Viral titers in AIDS subjects treated for wasting

Placebo vs HMB/Arg/Gln significantly different p<.01
Summary

- 250+ nutrition supplements marketed:
  - Only creatine and HMB meet scientific threshold for resistance exercise
  - ~Double effect
  - Short-term safety
  - New applications:
    - Rational Combinations
    - Targeted