2019 NSCA TACTICAL ANNUAL TRAINING

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I have no actual or potential conflict of interest in relation to this presentation.

Androgen and Nutrition Strategies to Promote Anabolism and Enhance Warfighter Lethality

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8/23/2019: 08:00 – 08:50 h

Learning Objectives

1. Identify mechanisms by which military operations degrade muscle mass and performance.
2. Define Warfighter nutrition requirements – do they differ from strength athletes?
3. This is not sanctioned competitive sports – this is war. Identify ethical and efficacious androgen therapies to enhance Warfighter lethality.

Characteristics and Consequences of Strenuous, Multi-Stressor Military Operations: Basis for Muscle Loss and Performance Decline

Learning Objective 1

Characteristics of Multi-Stressor Operations

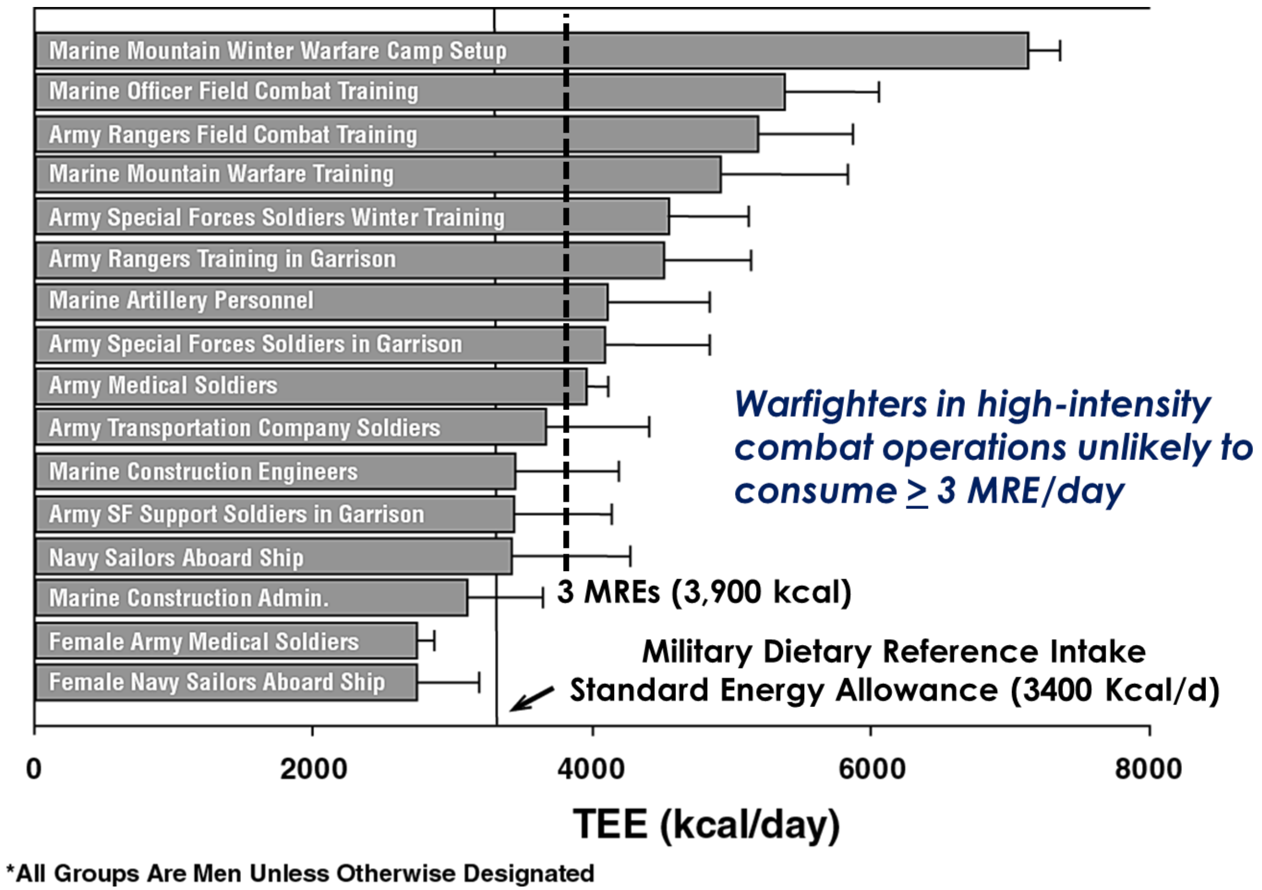
High Energy Expenditures
- Low intensity endurance movements
- Intermittent mod-high intensity work
- Prolonged periods (~20h/d)
- Carrying heavy weights

Physiological and Psychological Stress
- Limited food/energy deficits
- Disrupted/restricted sleep
- Physical and mental fatigue
- Diminished appetite

Environmental Extremes
- Austere locations
- Altitude, heat, cold

Consequences
- Diminished androgen status
- Increased stress/catabolic hormones
- Skeletal muscle loss
- Injury
- Physical/military performance decline
- Reduce readiness/jeopardize mission

Maintaining Energy Balance is Near Impossible



Tharion et al. Appetite. 2005

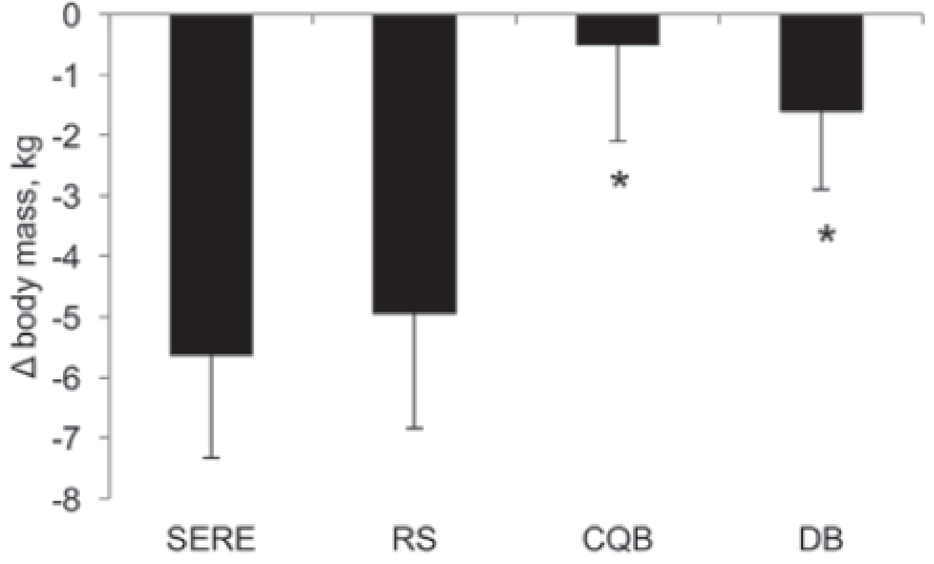
Energy Balance and Special Operations Training

Table 2 *TDEE, EI, and EB During the Field Phase of SERE School, Raider Spirit, Close-Quarter Battle, and Derna Bridge*

Energy Parameter, kcal/d	SERE, *n* = 10	RS, *n* = 12	CQB, *n* = 9	DB, *n* = 13
TDEE	4,011 ± 475	6,376 ± 712[a]	4,189 ± 476	3,754 ± 314
EI	346 ± 0[a]	2,410 ± 488	2,819 ± 488	2,702 ± 738
EB	–3,665 ± 475[a]	–3,966 ± 776[a]	–1,374 ± 683	–1,027 ± 740

Data given as mean ± standard deviation.
CQB, Close-Quarters Battle; DB, Derna Bridge; EB, energy balance; EI, energy intake; RS, Raider Spirit; SERE, Survival, Evasion, Resistance, and Escape; TDEE, total daily energy expenditure.
[a]Specific outcome measure different from other phases, $p < .05$.

Marine Corps Forces Special Operations

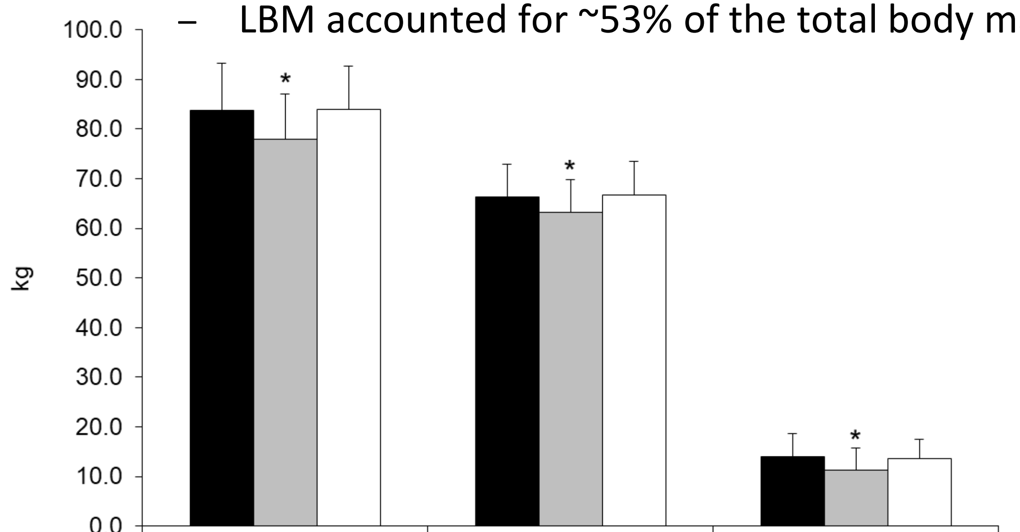


Sepowitz et al. J Spec Op Med. 2017

Lean Mass & Body Protein Loss during Military Operations

Body Composition

- ~7% reduction in total body mass
  - LBM accounted for ~53% of the total body mass lost.

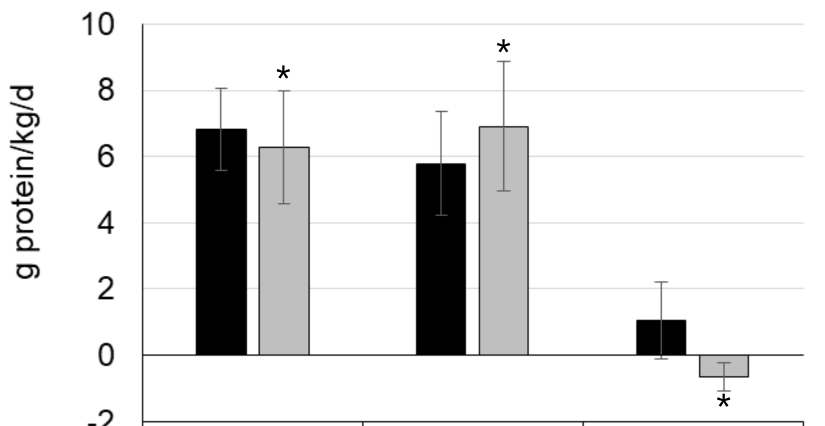


	Total Body Mass	Lean Body Mass	Fat Mass
■ BASELINE	83.8	66.3	14.0
■ POST-SERE	78.0	63.2	11.3
□ RECOVERY	83.9	66.8	13.6

Berryman et al. J Appl Physiol. 2017

Whole-Body Protein Turnover

- ~20% increase in protein breakdown
  - 160% decline in net protein balance.

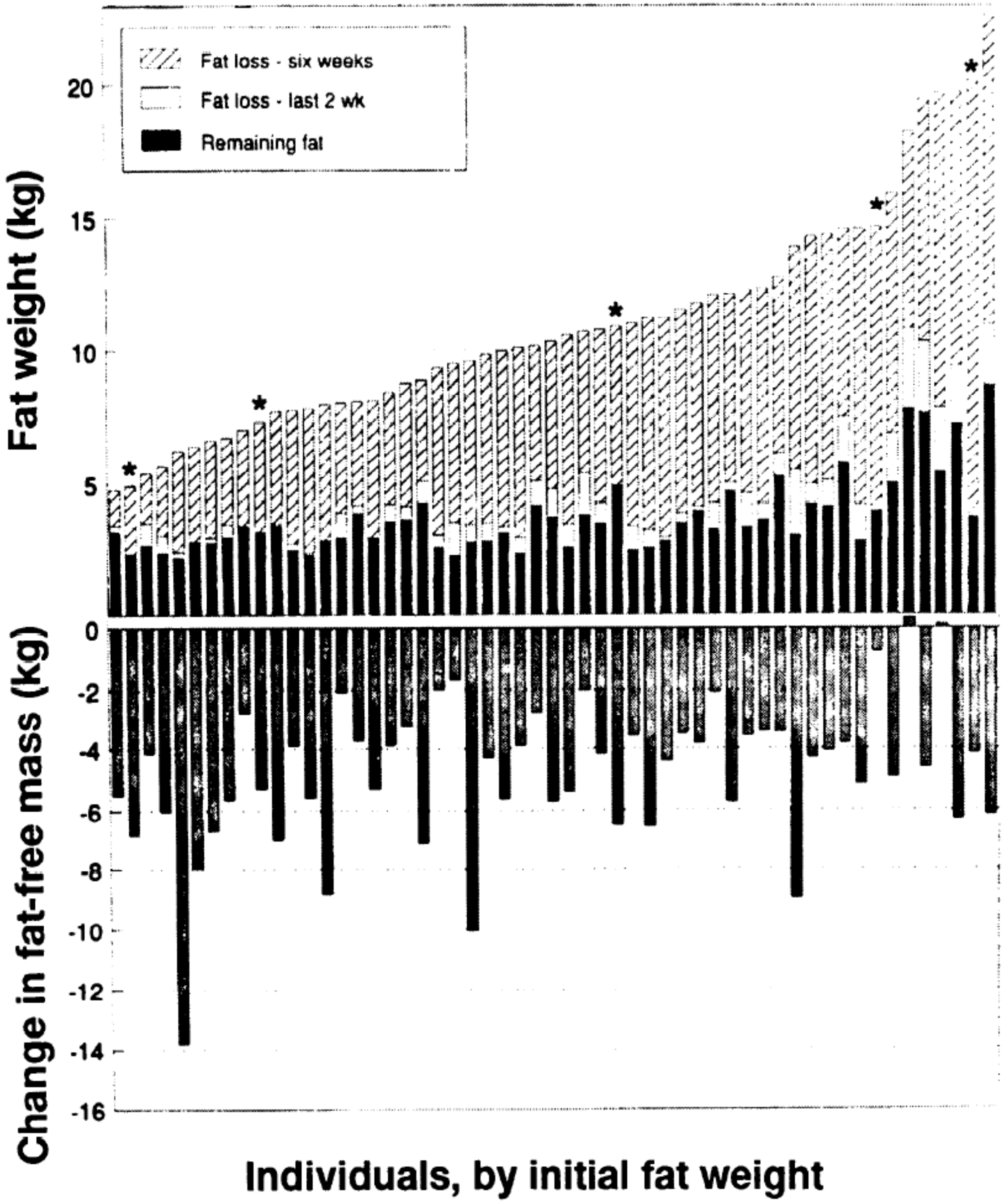


	Synthesis	Breakdown	Net
■ Baseline	6.84	5.79	1.05
■ POST-SERE	6.28	6.91	-0.64

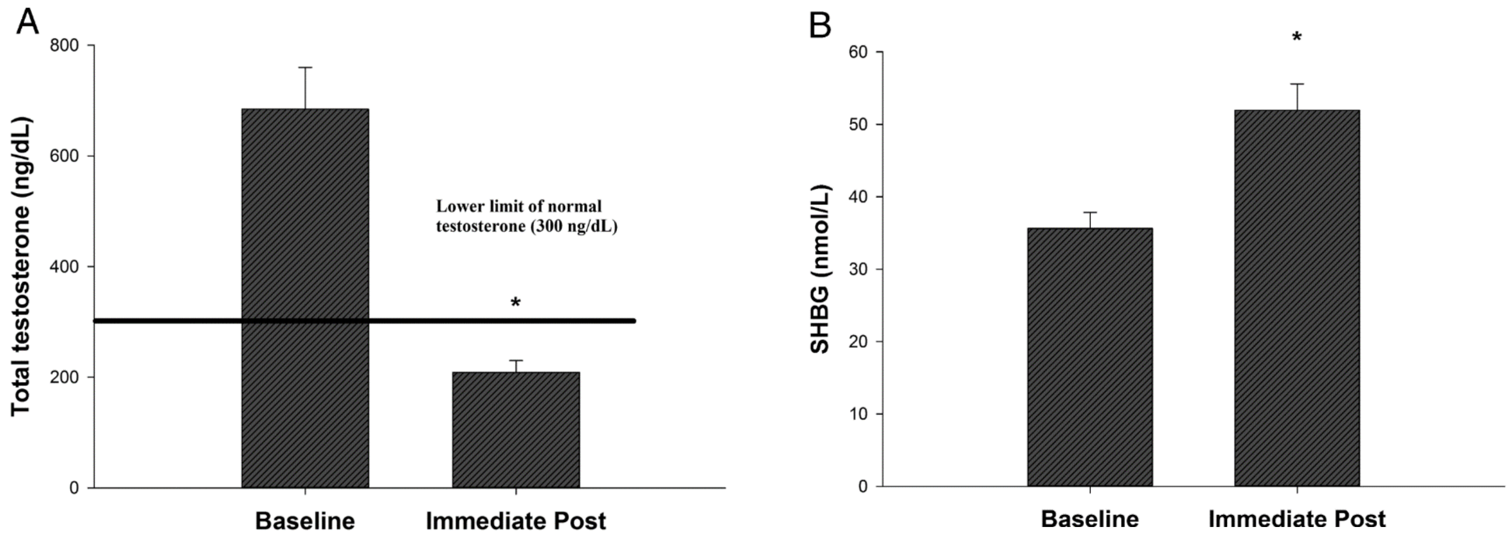
Lean Mass Loss cont.

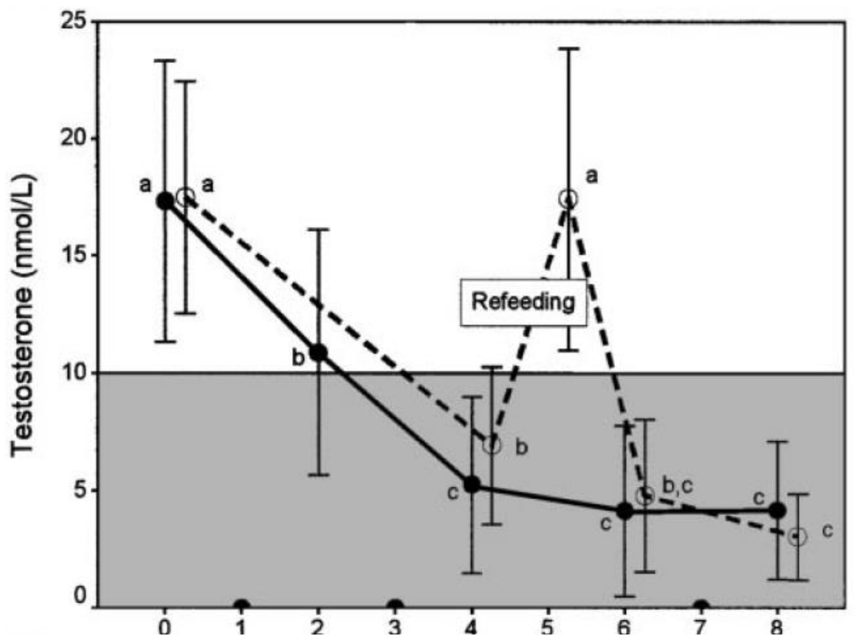
- Soldiers during US Army Rangers School:
  - 7-21 kg body mass loss, 0.3-14 kg was lean mass

Friedl et al. J Appl Physiol.1994



Multi-Stressor Military Operations Rapidly and Markedly Suppress the HPG Axis



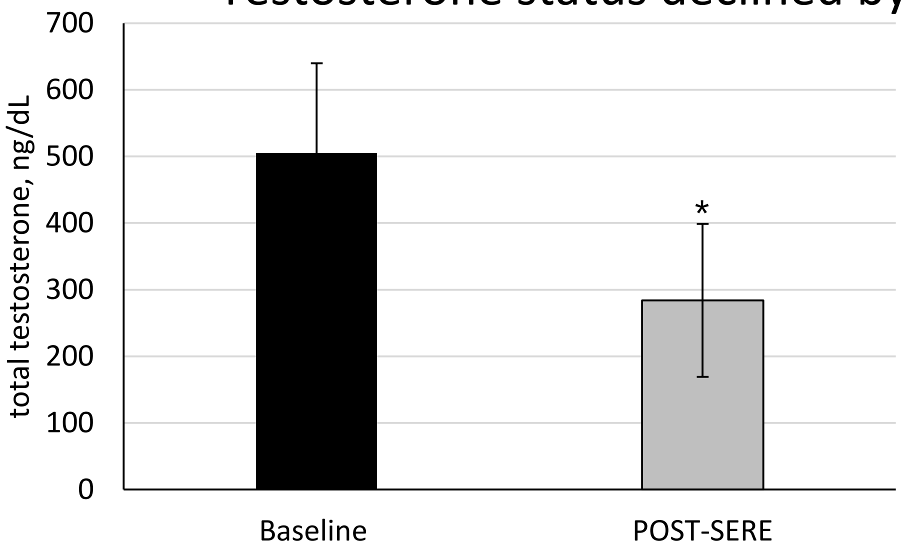


Henning et al. J Clin Endocrinol Metab. 2014

Friedl et al. J Appl Physiol. 2000

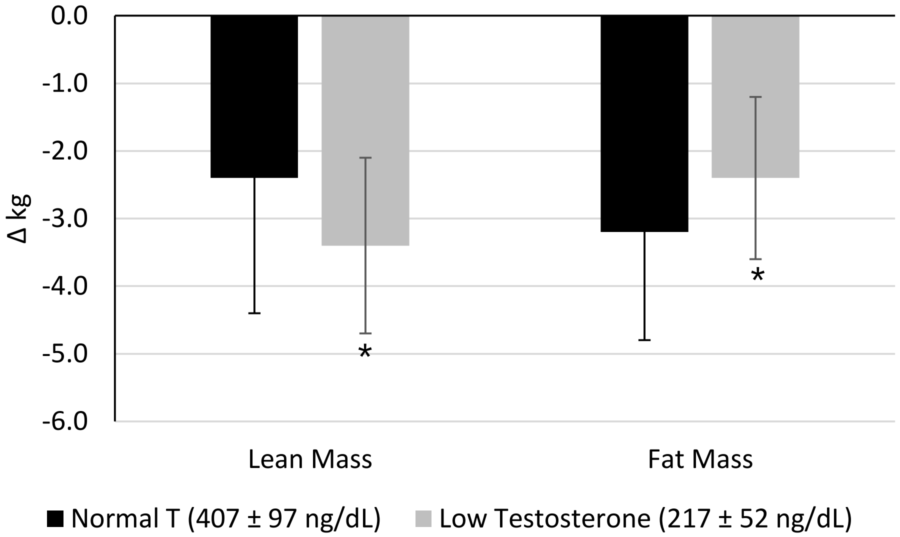
Testosterone Status and Lean Mass Loss

- Testosterone status declined by 44%



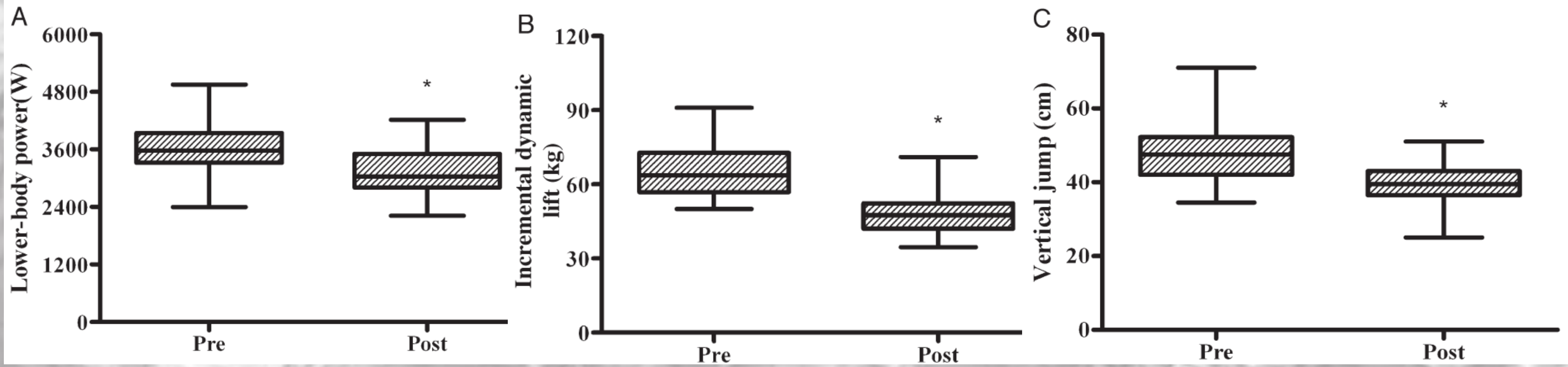
Berryman et al. unpublished

- Dichotomized into low and normal testosterone POST-SERE
  – LT lost more lean mass and less fat mass than NT



Military personnel susceptible to operational stress-induced low testosterone may be predisposed to greater lean mass loss during short-term, strenuous military training.

Physiologic Setting for Degraded Performance



Nindl et al. Med Sci Sport Exerc. 2007

Performance decrements associated ($r^2 = 0.48$) with energy deficit.

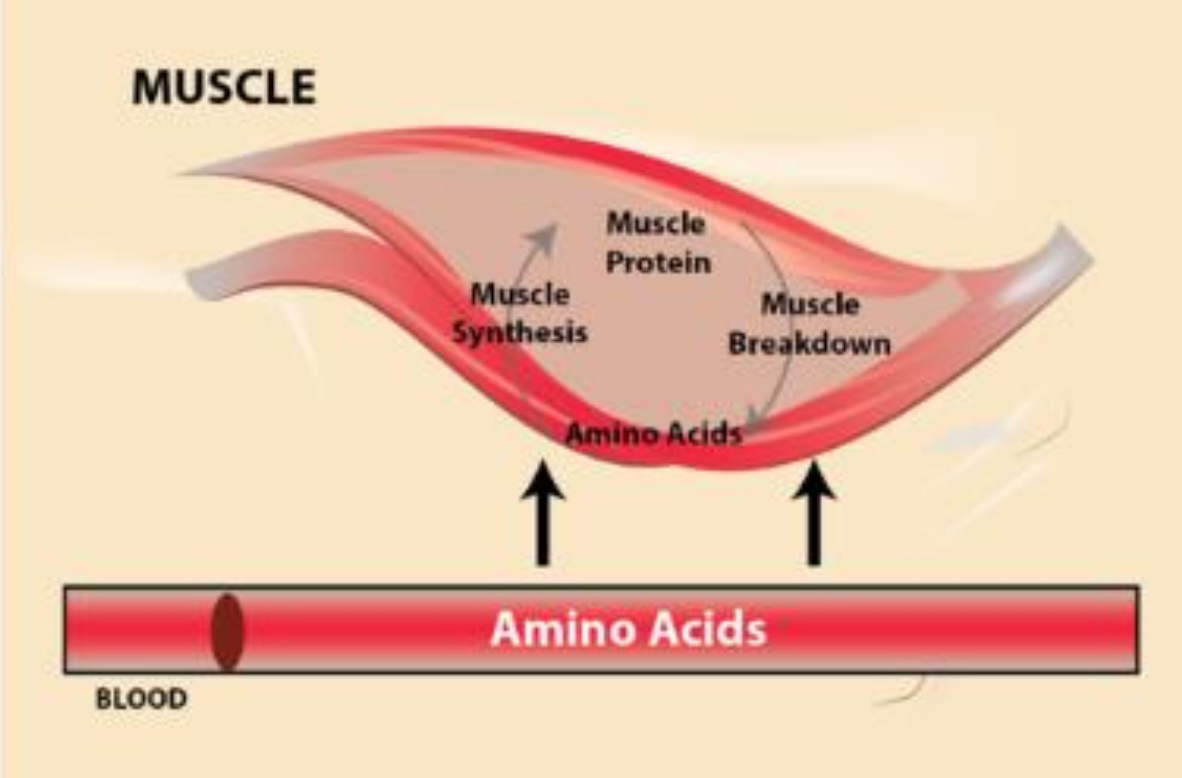
Murphy et al. Sport Med. 2018

Warfighter Nutrition Recommendations: Protein as a Countermeasure to Operational Stress

Learning Objective 2

Operational Stress and Muscle Mass Regulation

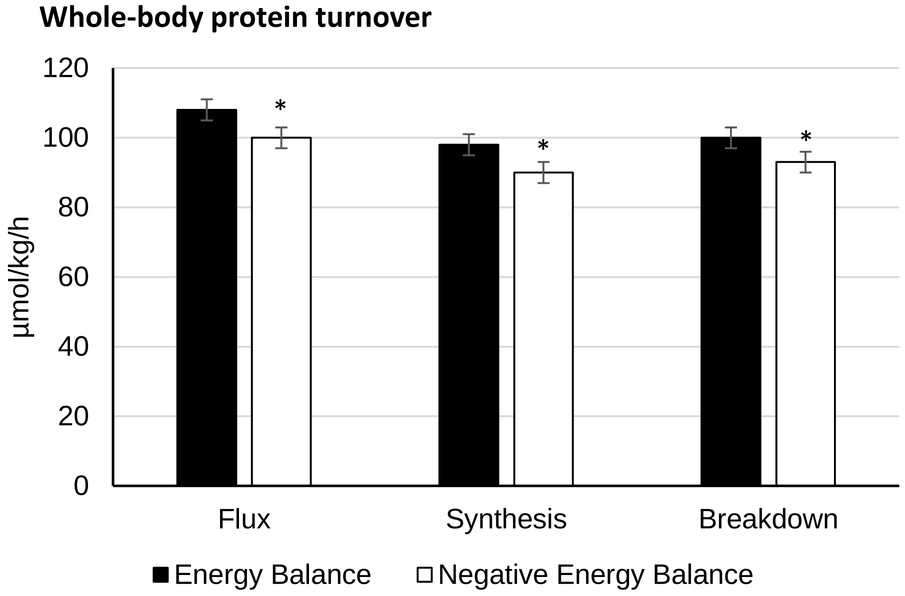
- Muscle is conserved when protein gained is equal to protein lost:
  - i.e., Synthesis = Breakdown
- Known sensitivity to some operational stressors:
  - Energy status
  - Protein
  - Exercise
  - Environment (hypoxia)



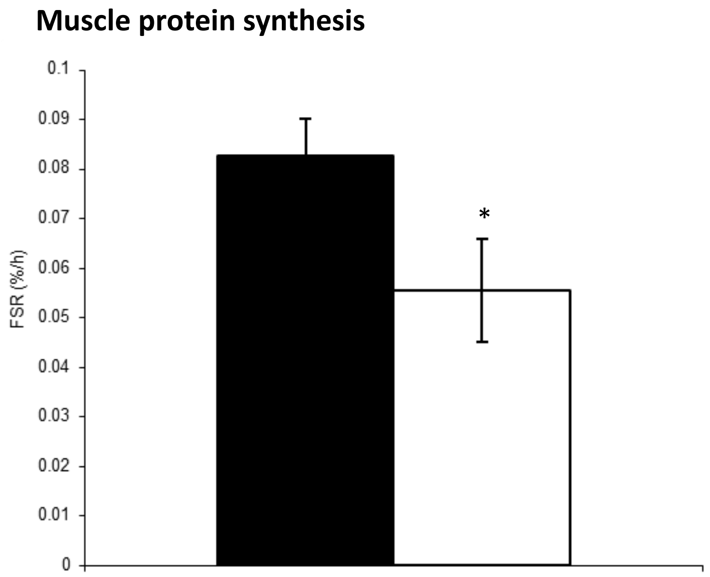
Regulated by several integrative signaling pathways.

Energy Deficit, Skeletal Muscle, and Whole-Body Protein Turnover

- Protein turnover (muscle and whole-body) is downregulated.



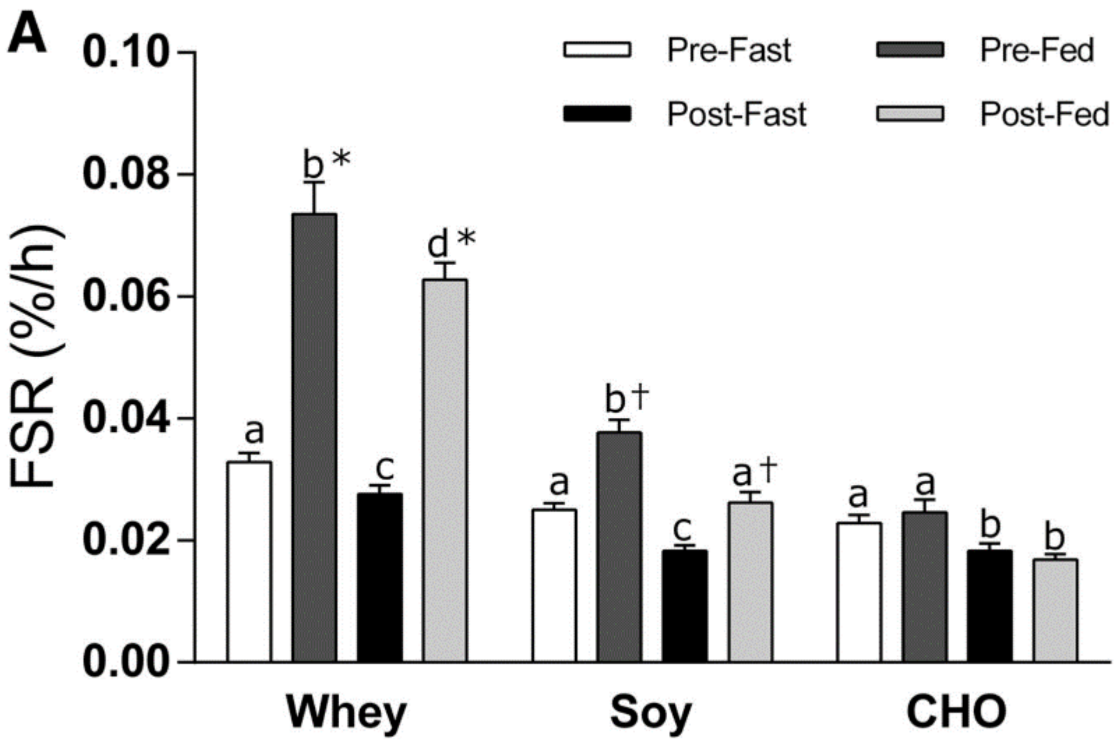
Pasiakos et al. Int J Obes. 2014
Stein et al. Metabolism. 1991



Pasiakos et al. J Nutr. 2010
Carbone et al. Appl Physiol Nutr Metab. 2014
Carbone et al. FASEB J. 2013

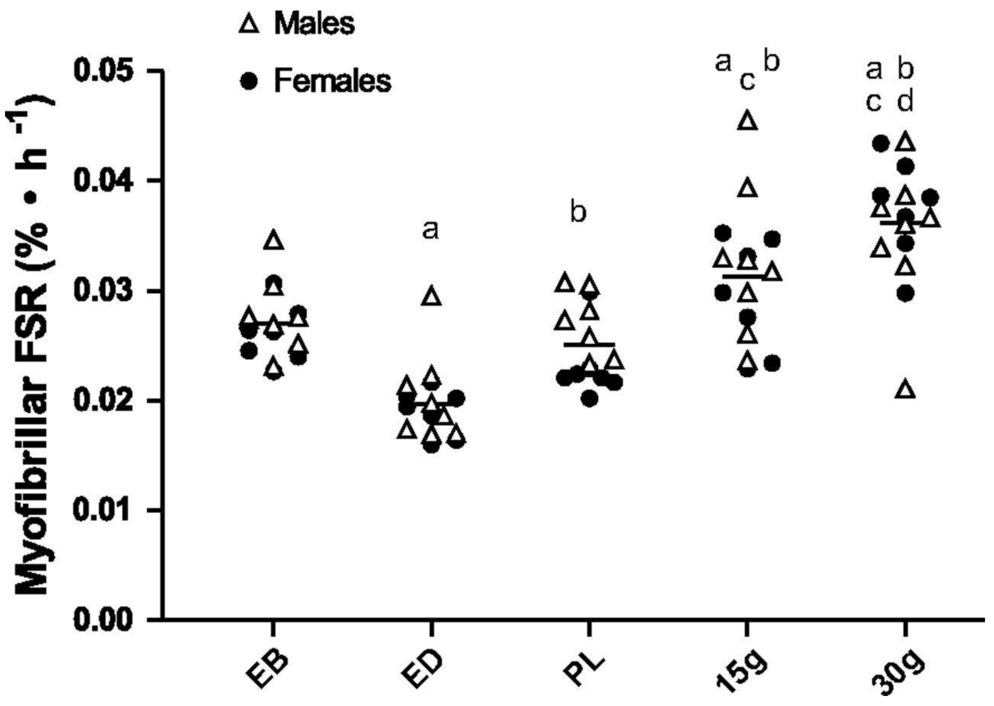
High-Quality Protein Ingestion Restores Muscle Anabolic Potential During Energy Deficit

- Ingesting high-quality protein attenuates declines in postprandial muscle protein synthesis during energy deficit.



Hector et al. J Nutr. 2015

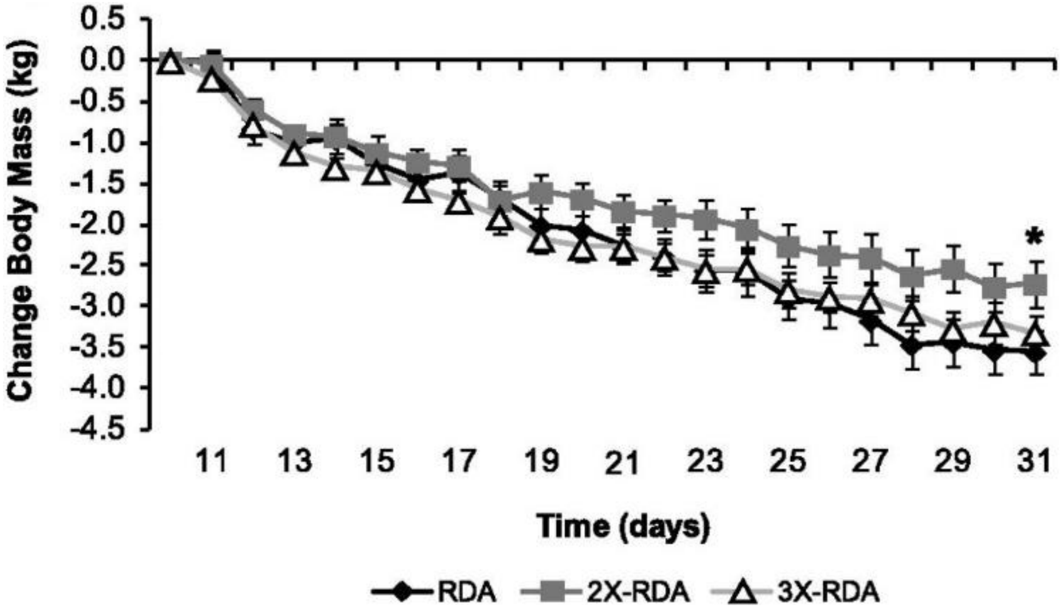
During “Normal” Weight Loss, Exercise and Protein Synergistically Benefit Muscle

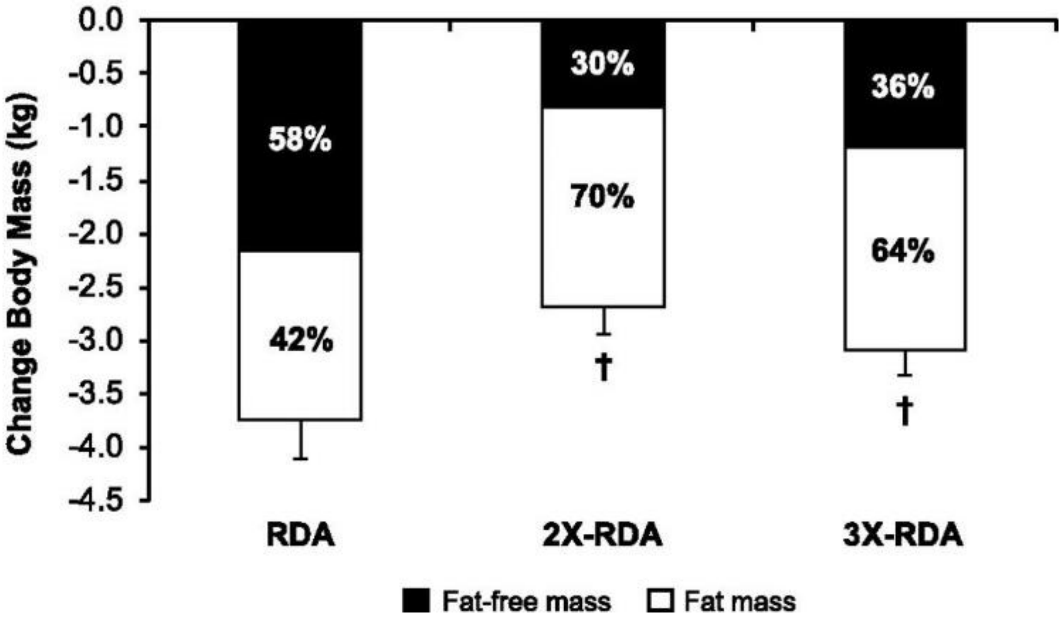


Areta et al. Am J Physiol Endocrinol Metab. 2014

- High-quality protein with exercise potentiates MPS restoration during energy deficit.

Energy Deficit: Effects of High Protein Diets

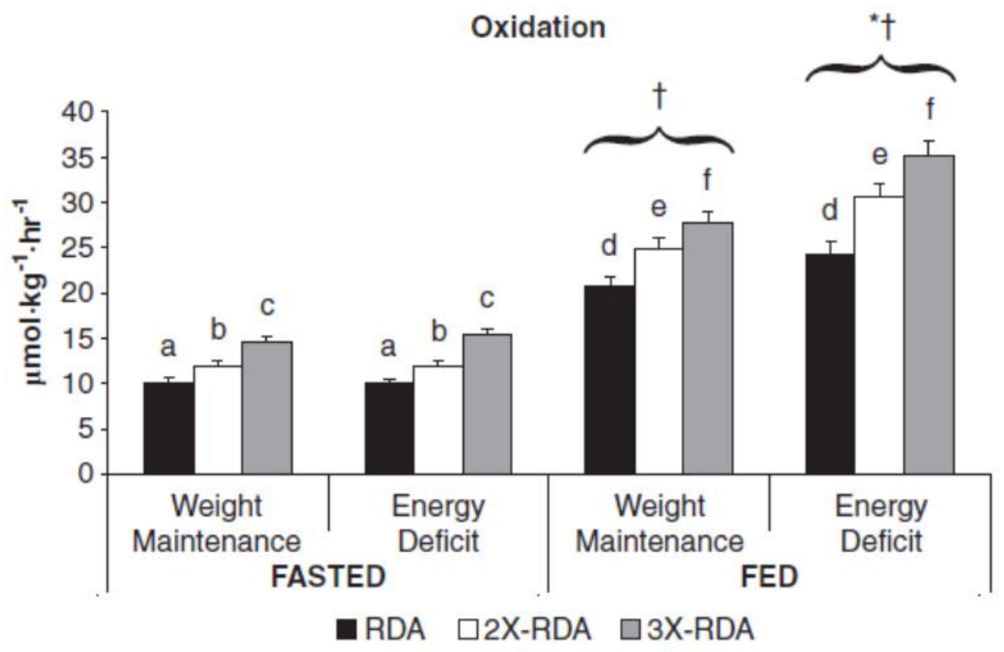




2X-RDA and 3X-RDA are equally effective during a 21 d diet- and exercise-induced, 40% energy deficit.

Pasiakos et al. FASEB J. 2013
Carbone et al. FASEB J. 2013

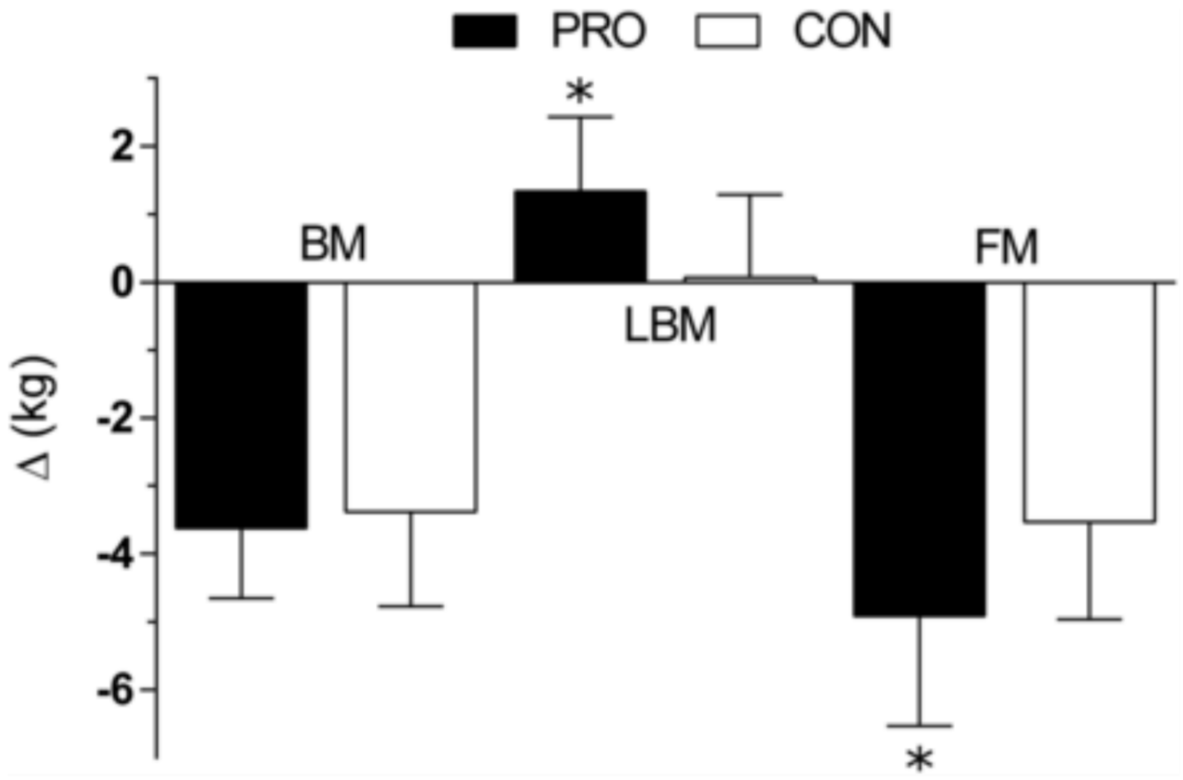
If More Protein is Good Than Even More Protein is Better during Moderate Energy Deficit



- Increased oxidative protein loss.
- No further lean mass protection.
- Exercise stimulus was minimal.
- Can more protein be beneficial if the exercise stressors were greater?

Pasiakos et al. Int J Obes. 2014

High Volume, High Intensity Exercise Potentiates Effects of Protein

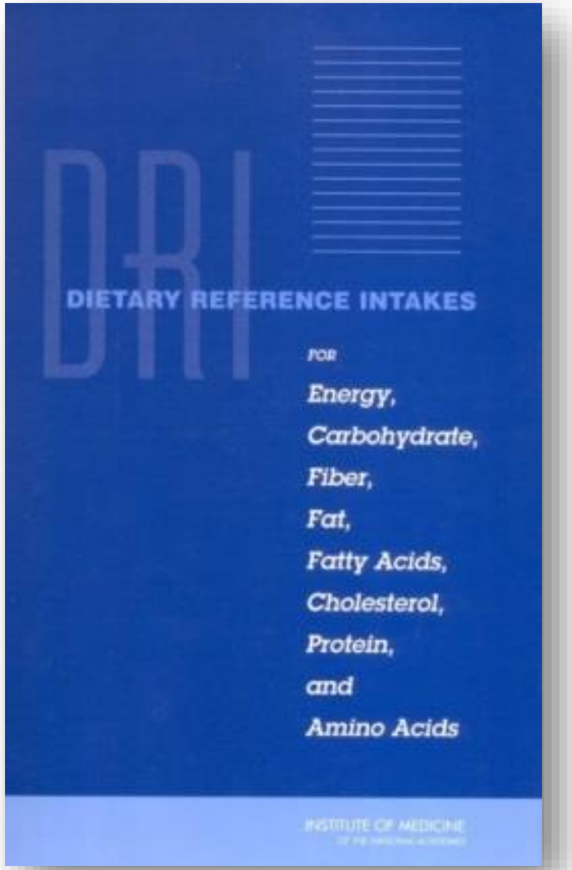


Longland et al. Am J Clin Nutr. 2016

- Advantages of 3X-RDA as compared to 1.5X-RDA are evident when high-quality, higher-protein diets are combined with HIT/SIT.

- Could the mechanical stress of exercise, coupled with higher-protein intakes, offset the catabolic effects of energy deficit?

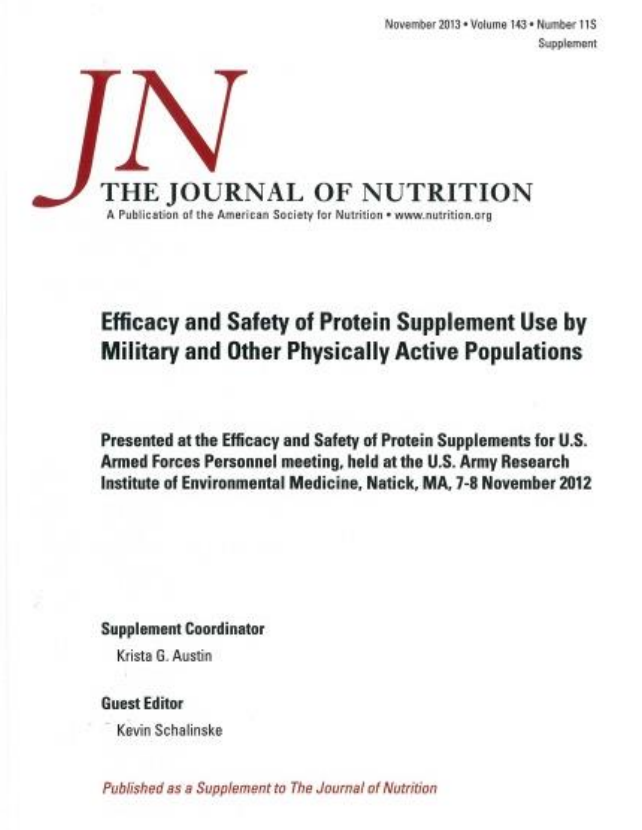
Countermeasure: Warfighter Protein Requirements



Army Regulation 40–25
OPNAVINST 10110.1/MCO 10110.49
AFI 44–141

Medical Services

Nutrition and Menu Standards for Human Performance Optimization


November 2013 • Volume 143 • Number 11S
Supplement

JN THE JOURNAL OF NUTRITION
A Publication of the American Society for Nutrition • www.nutrition.org

Efficacy and Safety of Protein Supplement Use by Military and Other Physically Active Populations

Presented at the Efficacy and Safety of Protein Supplements for U.S. Armed Forces Personnel meeting, held at the U.S. Army Research Institute of Environmental Medicine, Natick, MA, 7-8 November 2012

Supplement Coordinator
Krista G. Austin

Guest Editor
Kevin Schalinske

Published as a Supplement to The Journal of Nutrition

Warfighter vs. Sports Nutrition Protein Recommendations

	g/kg/d	Example Daily Protein Intakes, g	
		Male, 85 kg[6]	Female, 69 kg[6]
AR 40-25[1]	0.8-1.6	68-136	55-110
SME Consensus Statement[2]	1.5-2.0	128-170	104-138
ACSM/AND/D[3]	1.2-2.0	102-170	83-138
IOC[4]	1.2-1.6	102-136	83-110
ISSN[5]	1.4-2.0	119-170	97-138

[1]Army Regulation 40-25. 2017.
[2]Pasiakos et al. J Nutr. 2013.
[3]Thomas et al. *Med Sci Sport Exerc.* 2016
[4]IOC consensus statement on sports nutrition. *J Sports Sci.* 2011
[5]Jager et al. *J Int Soc Sport Nutr.* 2017
[6]Reference anthropometrics values characterize the averages of actual measurements attained from a 2007 pilot study of active and reserve duty Army Soldiers (Paquette, 2009).

Warfighters Generally Consume Enough Protein

Citation	Sample Size	Assessment Method	Protein Intake
Berryman et al. J Appl Physiol. 2017	63 US Marines attending SERE	24-h recall	2.0 g/kg/d
McClung et al. Appetite. 2017	131 US male Soldiers attending RASP	Digital food photography	1.9 g/kg/d
Margolis et al. Nutrients. 2012	209 US Army male (118) and female (91) Soldiers during Basic Combat Training	Food frequency questionnaire	1.0 g/kg/d
Margolis et al. Appl Physiol Nutr Metab. 2013	36 US Army Soldiers during SF training	Visual estimation	2.1 g/kg/d
Pasiakos et al. PLoS One. 2014	40 US Army male (37) and female (3) Soldiers	24-h recall	1.7 g/kg/d

No comprehensive database exists. Dietary intake data above are derived from small studies, with mixed methodologies, at various locations (dining facilities, off the economy), before or during training events, all of which could alter intake.

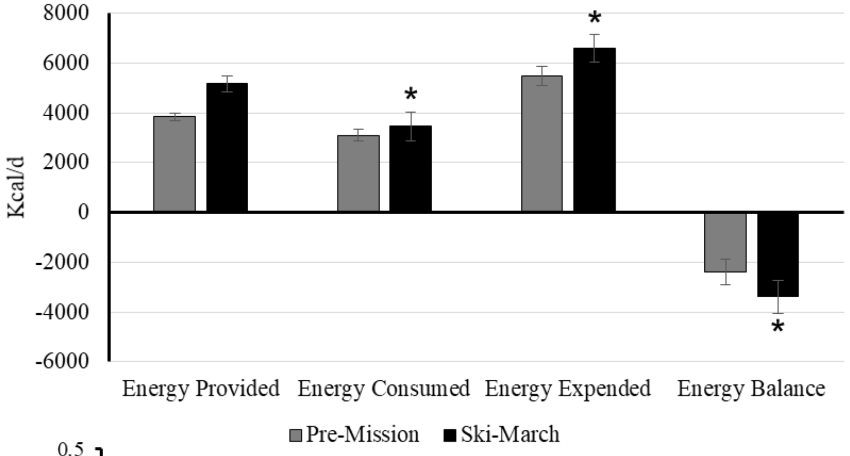
Regardless - protein intake exceeds minimum recommendations and appears to be at the upper-end of the protein intake range when access to food and time available to eat are not constrained by mission demands.

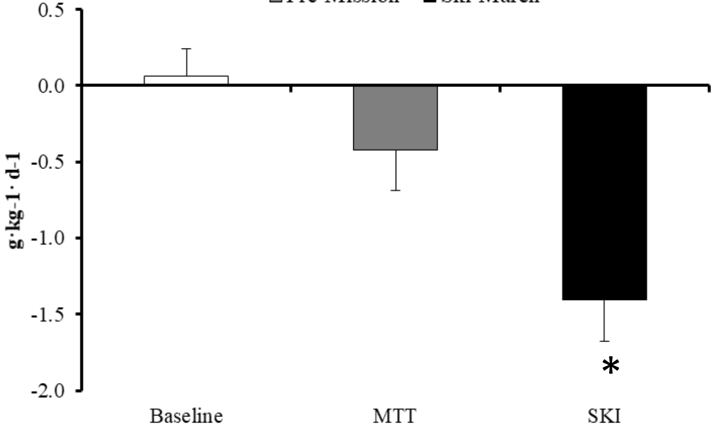
USARIEM

FFI Forsvarets forskningsinstitutt
Norwegian Defence Research Establishment

Field Demonstrations for Protein Recommendations

Recent findings from Training Operations

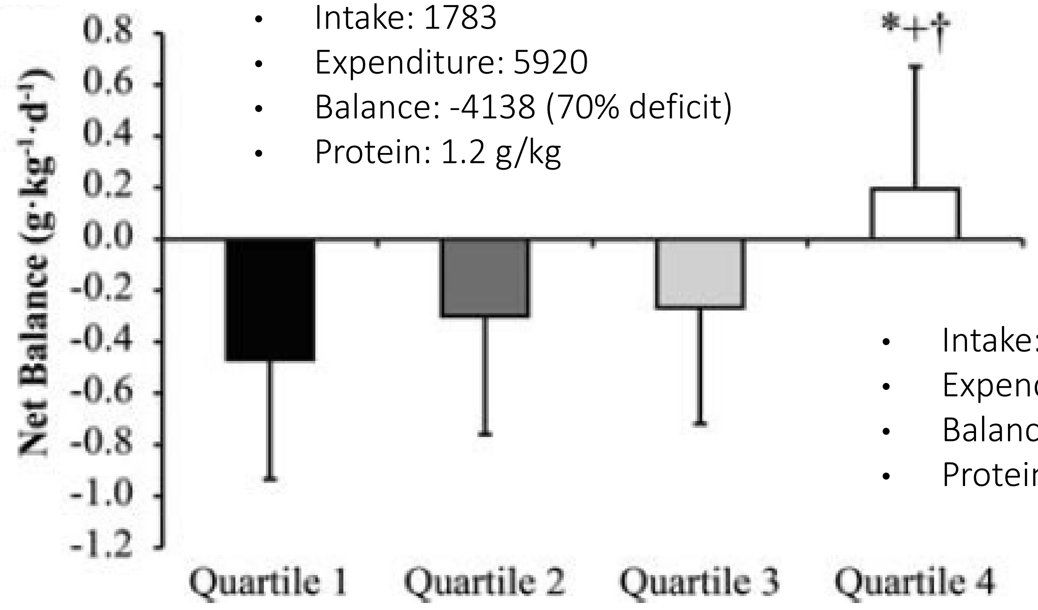




- 160-215 g (2.0-2.6 g/kg) protein provided
- 128-139 g (1.6-1.7 g/kg) protein consumed
- Deficits would have been 25-30% if the rations were consumed in their entirety
- 800-1500 Kcal/d thrown away/not consumed, resulting in deficits ~50% (2500-3000 Kcal/d)
- Protein retention became progressively more negative

Margolis et al. Appl Physiol Nutr Metab. 2014

Efficacy of Higher-Protein Diets is Diminished by Severe Energy Deficits



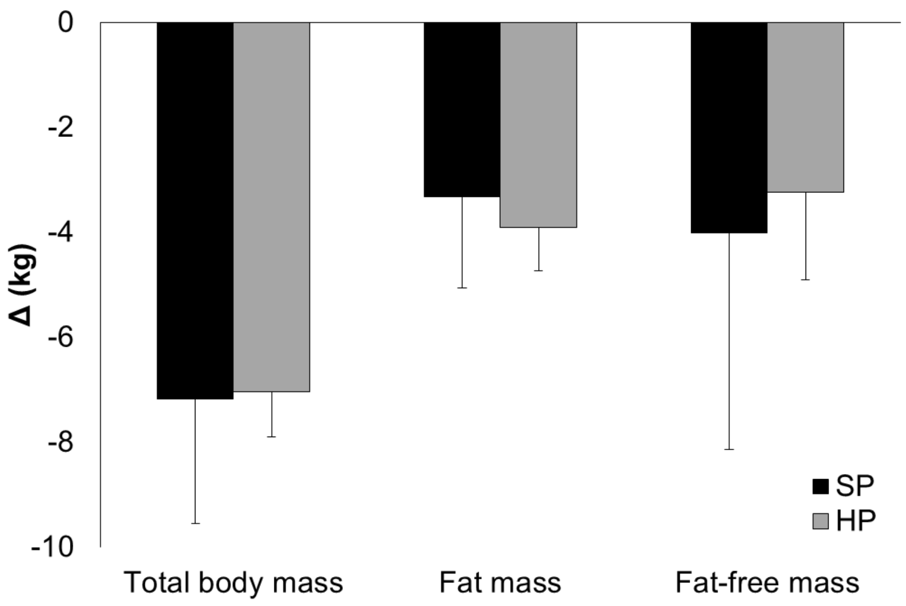
- Intake: 1783
- Expenditure: 5920
- Balance: -4138 (70% deficit)
- Protein: 1.2 g/kg

- Intake: 3723
- Expenditure: 6133
- Balance: -2410 (40% deficit)
- Protein: 2.1 g/kg

- Greater protein intakes are ineffective when energy deficits exceed 40% of daily energy needs. Protein then becomes a readily available source of fuel.

Margolis et al. Med Sci Sport Exerc. 2016

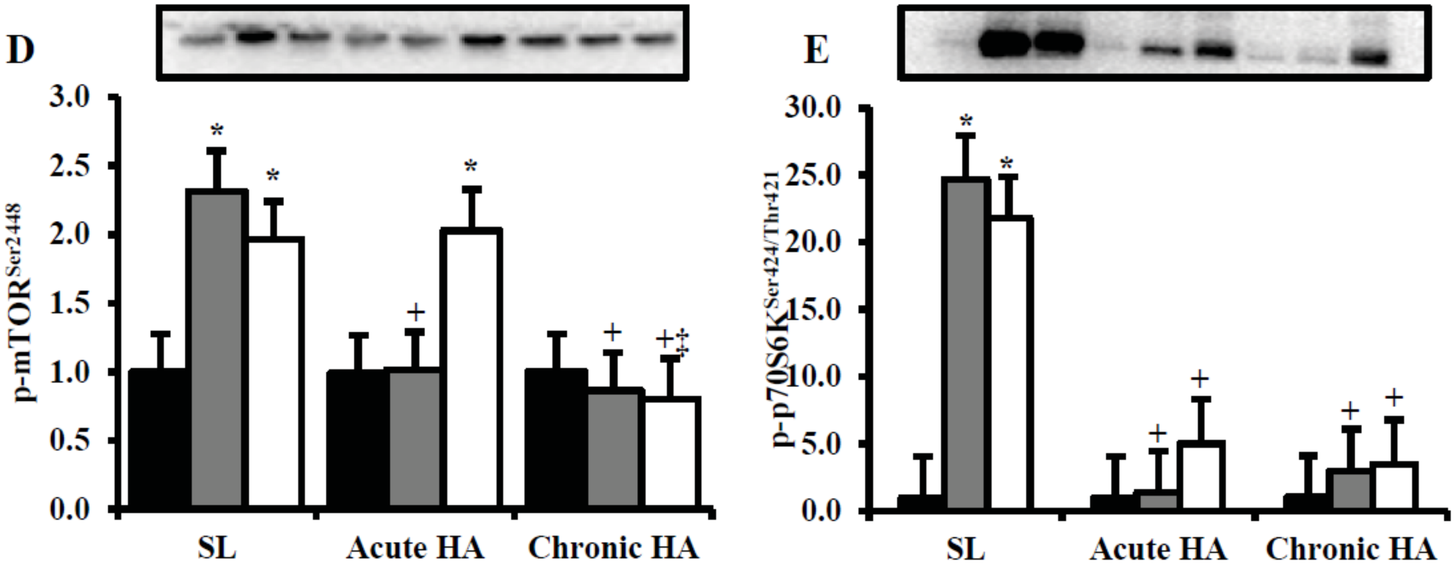
Operationally-Relevant Environmental Stress



Berryman et al. FASEB J. 2018

- Higher protein diets did not spare lean mass during energy deficit at high altitude because muscle anabolic sensitivity was suppressed and energy expenditure and protein oxidation were upregulated.

Hypoxia- and Energy Deficit-Mediated Anabolic Resistance



- HA exposure and energy deficit inhibit mTORC1 signaling.
- No change in proteolysis.

Margolis et al. FASEB J. 2018

Values are mean ± SEM. Within [BASE (■), POST (■), and REC (□)] and between study phase (SL, Acute HA, and Chronic HA) responses to exercise and whey protein ingestion for p-mTOR^{Ser2448} and p-p70S6K$^{Ser424/421}$. +Different than SL, ‡different than Acute HA, and *different then BASE, phase-by-time interaction, $P < 0.05$.

Learning Objective 2: Summary

Protein recommendations:

- 0.8-2.0 g/kg (AR40-25, Pasiakos et al. J Nutr. 2013).
- Warfighters generally consume enough protein – when access and time to eat are not limited.

Efficacy:

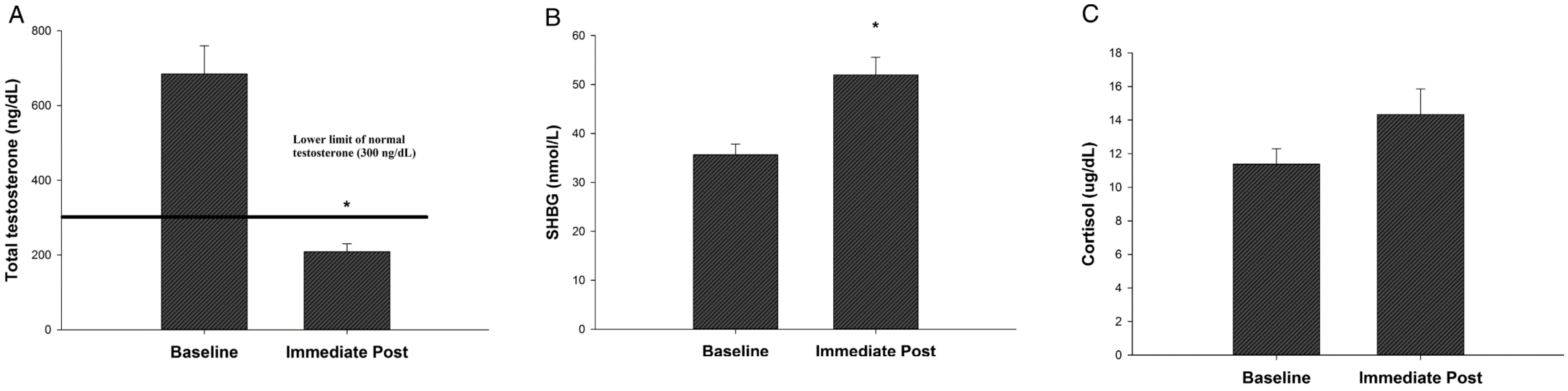
- Higher-protein diets, particularly when combined with resistance exercise, will spare lean mass during moderate energy deficit.
- Higher-protein diets may not be effective when energy deficits are more extreme, or when Warfighters are exposed to hypoxia.
- Goal should be to prioritize energy intake.

Biomedical Performance Enhancement: Potential Benefits of Supplemental Testosterone

Learning Objective 3

Operational Stress and Testosterone Revisited

- Prolonged operational stress:
  - Suppresses endogenous testosterone synthesis.
  - Limits bioavailable free testosterone.
  - Promotes a stress-induced catabolic state.
- Recovery is variable - ~30 days.



Henning et al. J Clin Endocrinol Metab. 2014

Considerations for Testosterone Treatment

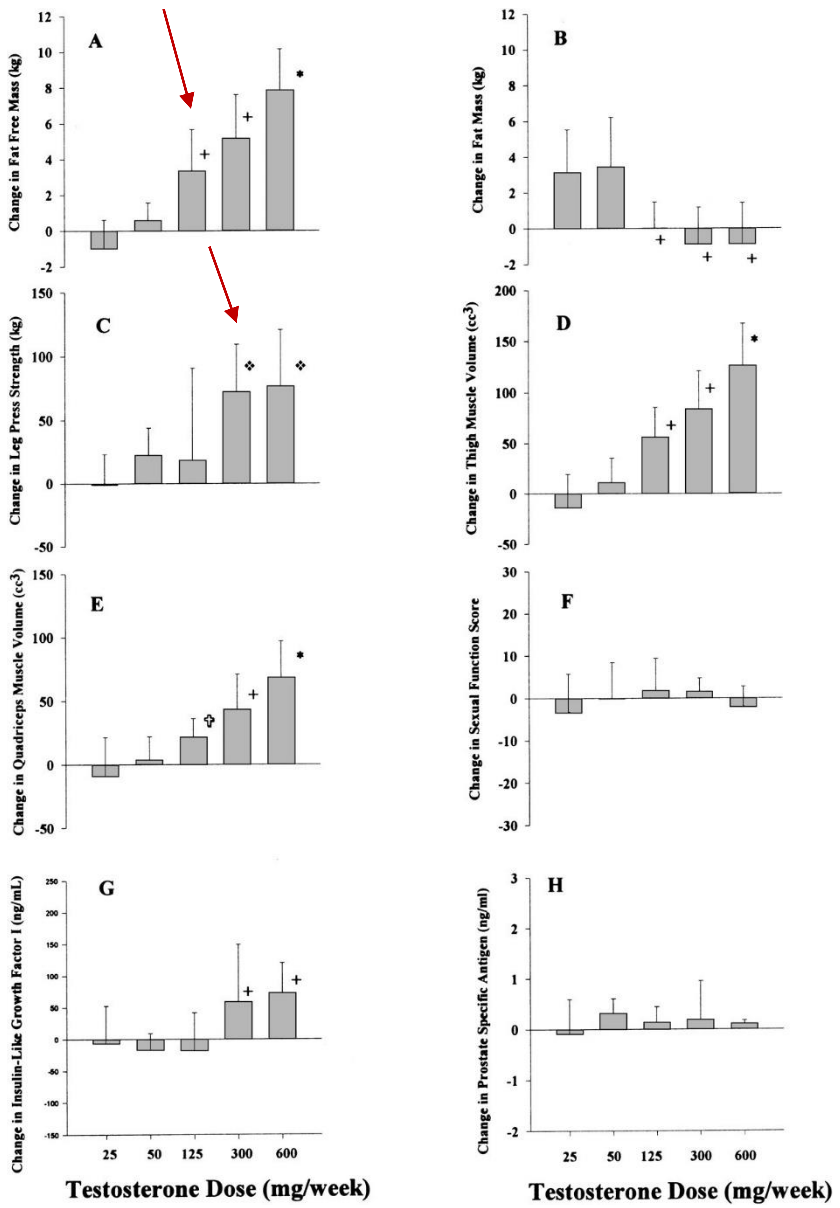
- Ethical considerations
  - Controlled substance and hormonal administration to a "healthy" adult
  - Male specific treatment option
  - Cognitive/behavior (i.e., aggression)
- Safety considerations
  - Lipids
  - Erythrocytosis
  - Cardiovascular
  - Acne
  - Male-pattern baldness
  - Gynecomastia
  - Hepatic function
  - Prostate enlargement
  - Endogenous recovery after treatment cessation

- Efficacy
- Will it work?
- How will it be administered?
- Is it safe?

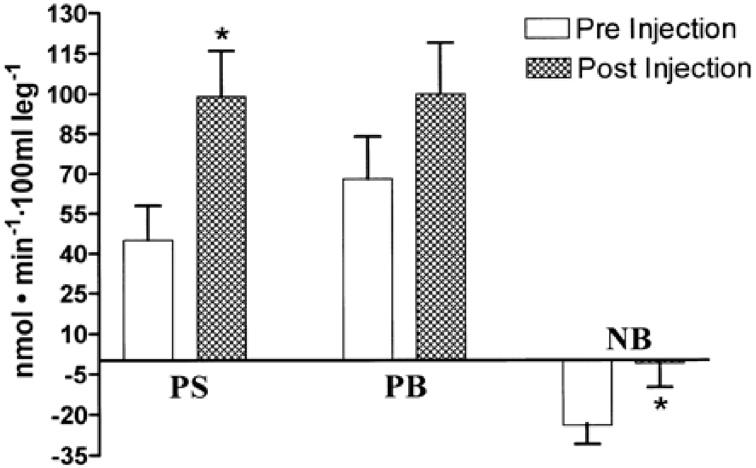
Clinical Efficacy

- Healthy men, 18-35 y provided weekly doses of testosterone enanthate for 20 wk following GnRH agonist administration.

Bhasin et al. Am J Physiol Endocrinol Metab. 2001



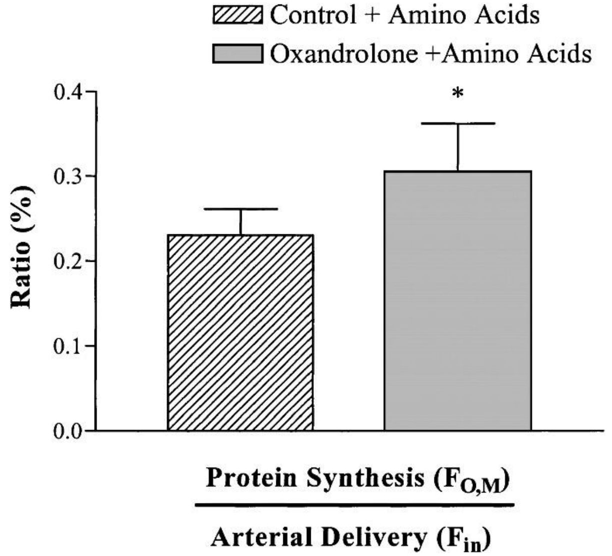
Enhanced Protein Synthetic Efficiency and Restoration of Muscle Anabolic Sensitivity to Nutrition



Ferrando et al. Am J Physiol. 1998

5-d testosterone administration (200 mg) in healthy men increased PS and NB without increasing inward transport of amino acids, suggesting an increased efficiency of reutilization of amino acids from protein breakdown.

Expressing synthesis relative to amino acid delivery to the leg, which was lower for Ox+AA, a combined effect of oxandrolone and amino acids was seen compared with amino acids alone.



Sheffield-Moore et al. Am J Physiol. 2000

Clinical Safety

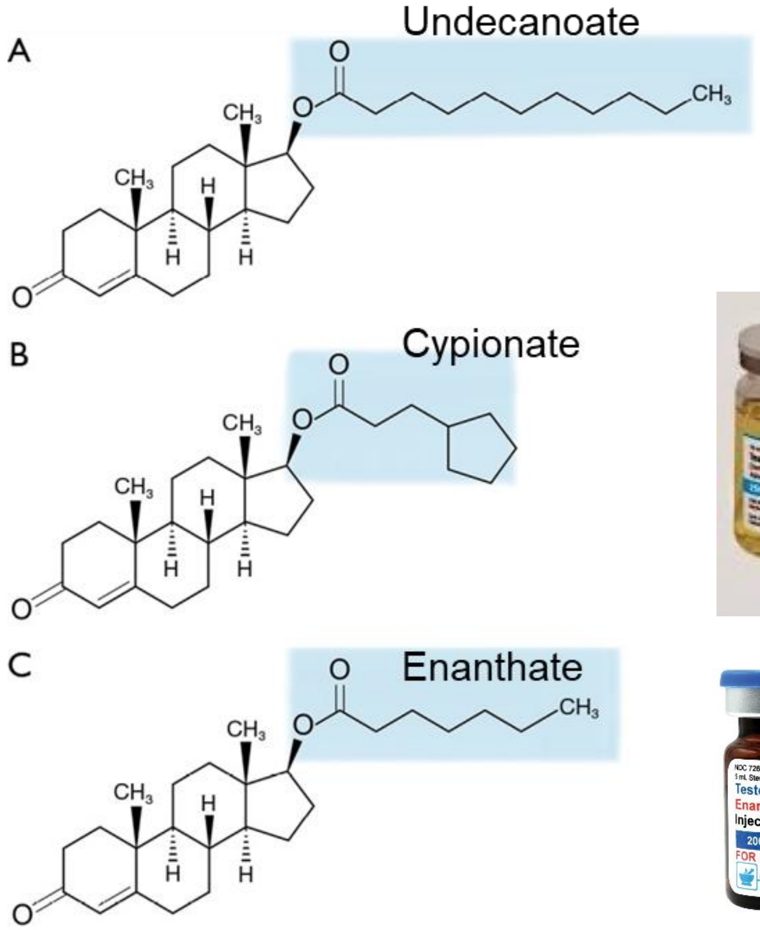
Lessons From the Testosterone Trials

Snyder et al. Endo Rev. 2018

Table 2. Adverse Events During 1 Year of Treatment in TTrials

Event	Treatment: Placebo	Treatment: Testosterone
Participants, n	394	394
Prostate events, n		
PSA increase ≥1.0 ng/mL	8	23
Prostate cancer	0	1
IPSS >19	26	27
Hemoglobin ≥17.5 g/dL	0	7
CV events,[a] n		
MI (definite/probable)	1	2
Stroke (definite/probable)	5	5
CV death	1	0
Total (MI, stroke, CV death)	7	7
Serious adverse events		
Death	7	3
Hospitalization	78	68
Other[b]	6	7

Lots of Options for Testosterone – What is Feasible for Operational Use?



TESTOPEL® 75mg
(testosterone pellets) CIII

Natesto®
(testosterone) nasal gel CIII

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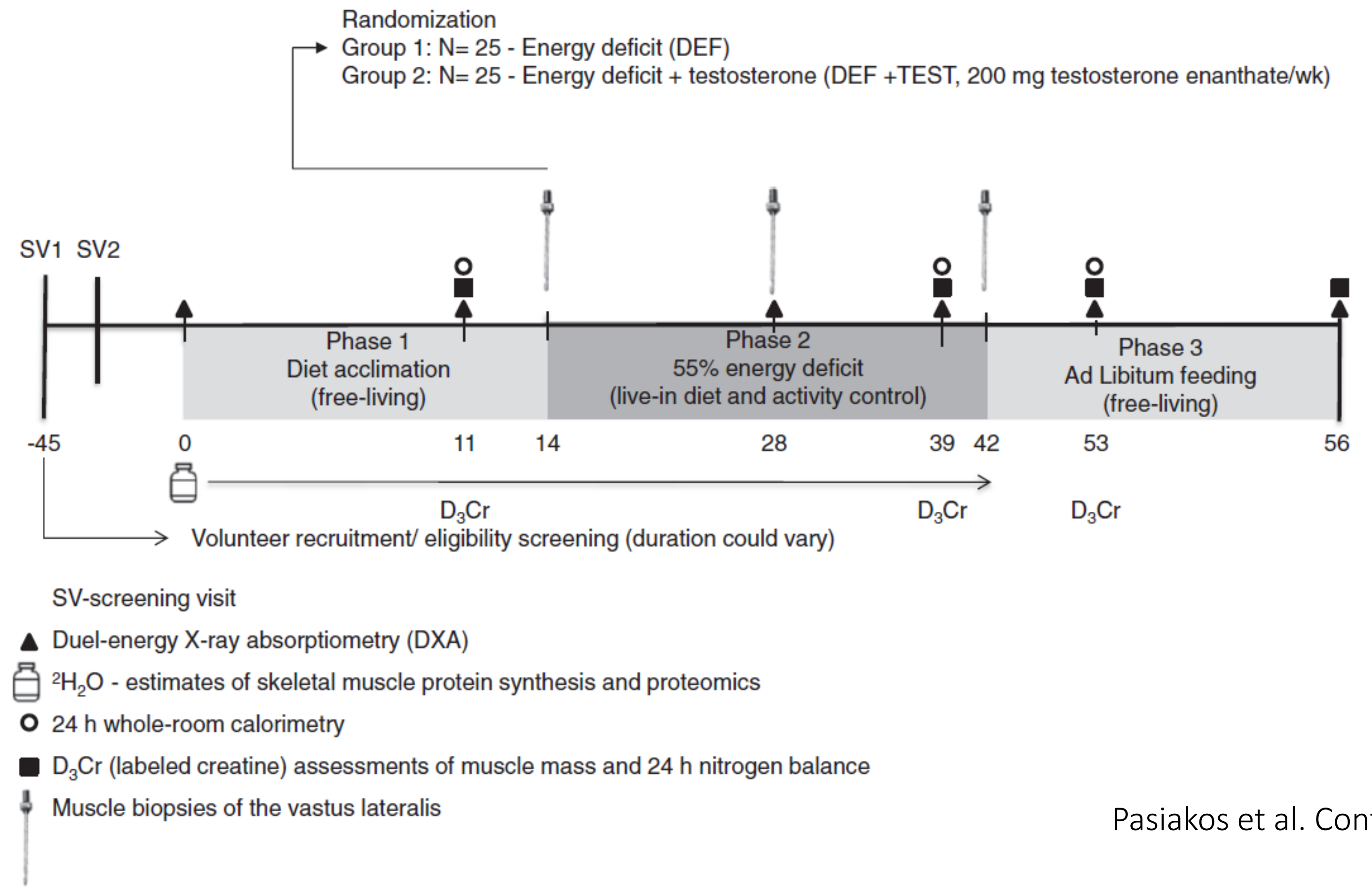
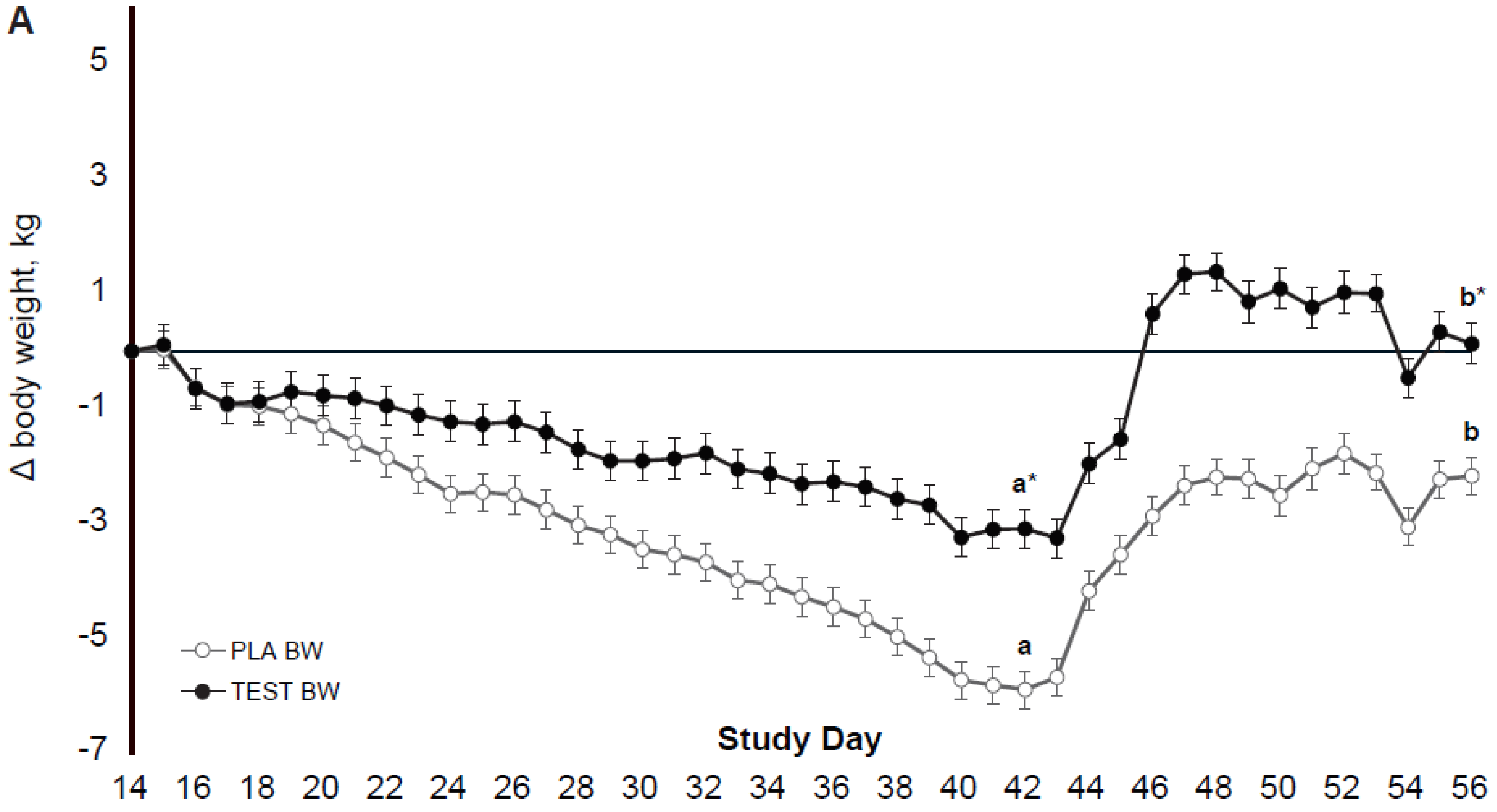
OPS
OPTIMIZING PERFORMANCE FOR SOLDIERS

OPS Experimental Design



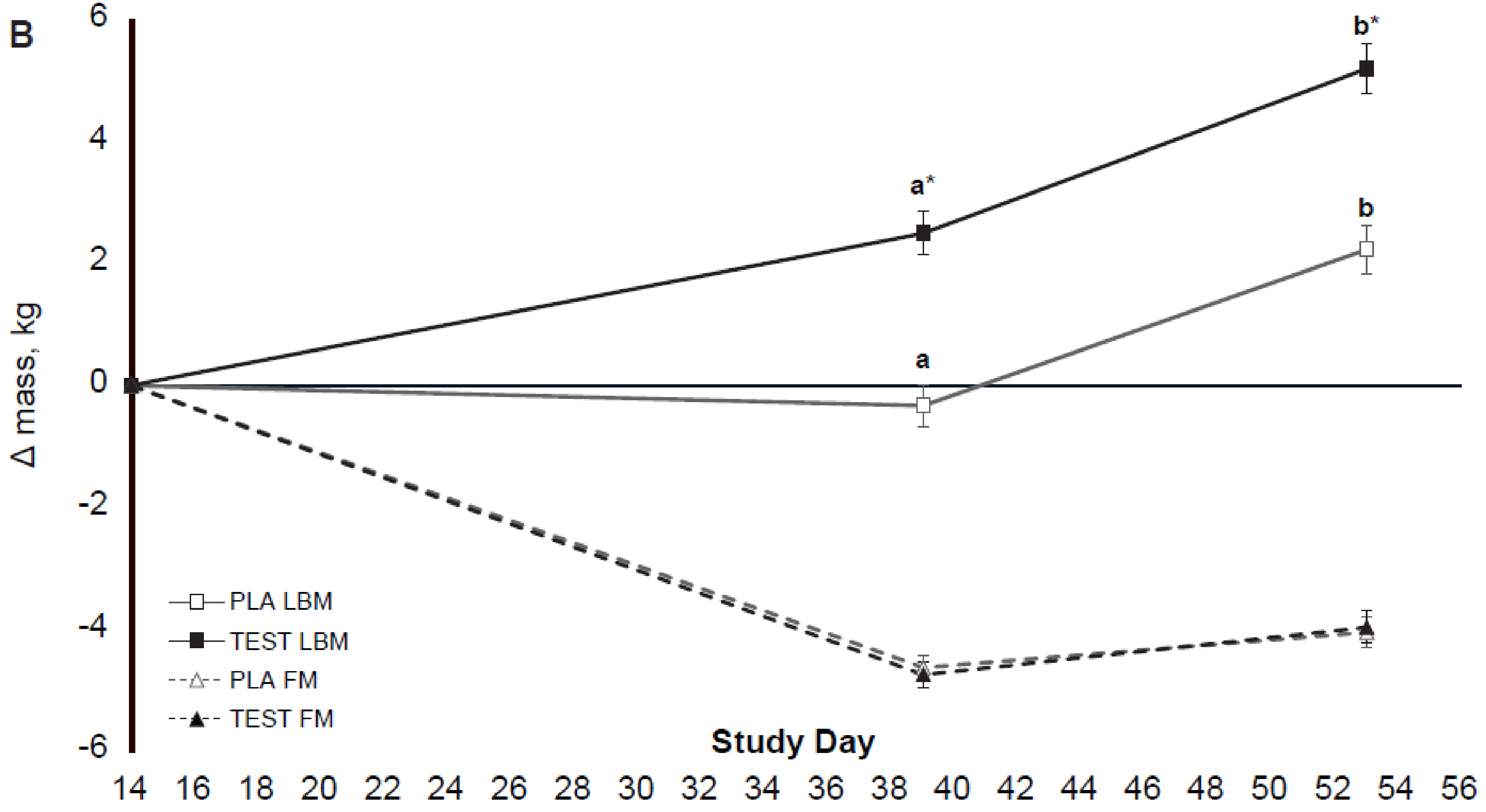
Pasiakos et al. Cont Clin Trial. 2017

Testosterone Supplementation Minimized Weight Loss During Severe Exercise- and Diet-Induced Energy Deficit



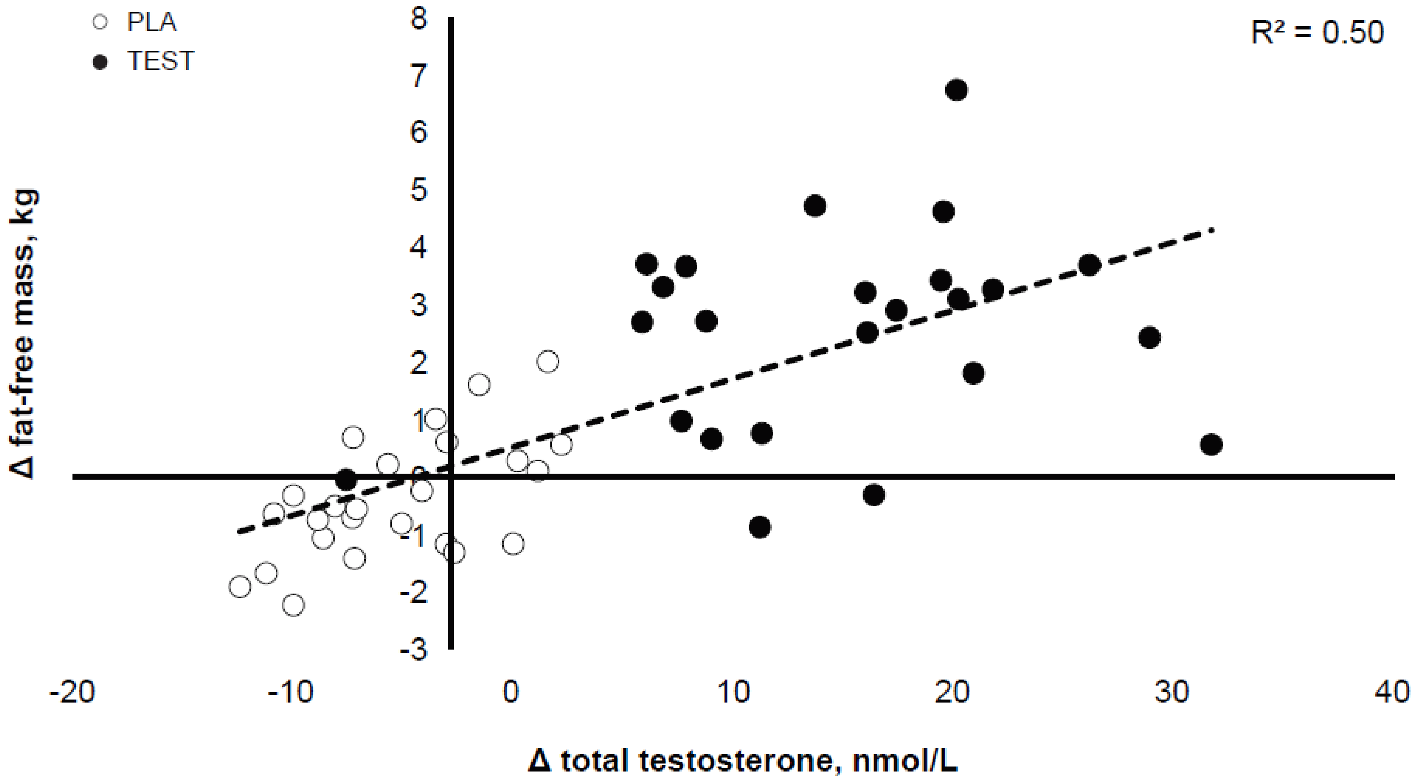
Pasiakos et al. in review.

Testosterone Restoration Enhanced Lean Mass



Pasiakos et al. in review.

Change in Total and Free Testosterone Strongly Associated with Change in Lean Mass



Pasiakos et al. in review.

Muscle Strength and Endurance Unaffected

	TEST (n=24)			PLA (n=26)			P-value		
	P1	P2	P3	P1	P2	P3	Phase	Treat	P x T
Isometric torque									
Peak, Nm[4]	245 (221, 269)	219 (195, 243)	214 (190, 238)	243 (220, 266)	219 (196, 243)	229 (205, 252)	< .0001	.78	.37
Peak, Nm/kg LBM[4]	24 (22, 26)	21 (19, 23)	20 (18, 22)	26 (24, 28)	24 (22, 26)	24 (22, 26)	< .0001	.014	.31
Isokinetic torque									
Peak, Nm[4]	200 (181, 219)	164 (145, 183)	174 (155, 193)	195 (177, 213)	163 (145, 181)	168 (150, 186)	< .0001	.72	.82
Peak, Nm/kg LBM[4]	20 (18, 21)	16 (14, 17)	16 (14, 17)	21 (19, 22)	17 (16, 19)	17 (16, 19)	< .0001	.12	.72
Total work, J[1]	3339 (3024, 3653)	2800 (2485, 3115)	3180 (2865, 3494)	3423 (3121, 3726)	2843 (2541, 3146)	2985 (2683, 3288)	< .0001	.91	.26
Total work, J/kg LBM[4]	327 (303, 352)	266 (242, 290)	291 (267, 316)	362 (339, 385)	306 (282, 329)	307 (284, 331)	< .0001	.033	.33

Values are least squares mean (95% confidence interval). Main effect of phase, [1]all phases are different; , [4]P1 is different than P2 and P3.

Pasiakos et al. in review.

Learning Objective 3: Summary

Supplemental Testosterone Restoration for Biomedical Performance Enhancement

- 200 mg of testosterone enanthate per week, per 4 weeks, did not increase health-related risk.
- Enhanced lean mass and limited body mass loss with exercise- and diet-induced energy deficit.
- No apparent muscle functional benefit (i.e., isokinetic/isometric dynamometry).

Bottom Line: Jury is Still Out.

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- US Army Special Forces
- US Marine Corps Mountain Warfare Training Center
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