Optimize Protein, Maximize Muscle: Keys to Preventing Disease and Promoting Wellness

A webinar with Functional Nutritionist
Robert Iafelice, MS, RDN

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Disclosure to Participants

Notice of Requirements For Successful Completion

- Please refer to learning goals and objectives
- Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours

Conflict of Interest (COI) and Financial Relationship Disclosures

- No conflicts to disclose

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Robert Iafelice, MS, RDN

Robert Iafelice, MS, RDN is a functional nutritionist and freelance medical writer. In addition to “Hold on to Your Muscle, Be Free of Disease,” Robert has written continuing education programs for nutritionists on topics like intermittent fasting and food allergies and intolerances. Robert received a Bachelor of Arts degree in Chemistry from Miami University in Oxford, Ohio, and a Master of Science degree in Nutrition Science from Case Western Reserve University in Cleveland. Most of his experience as a practicing registered dietitian was in the field of integrative/functional medicine with a focus on food allergy.

Robert’s diverse background also includes extensive experience in fitness/wellness as a gym owner, university nutrition instructor, health educator in the nutraceuticals industry, and oncology. As a fitness enthusiast, he competes in Masters track & field events.

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Learning Objectives

At the conclusion of this webinar, the learner will be able to:

1. State the four metabolic functions of muscle
2. State the three major triggers of muscle protein synthesis (MPS)
3. State the ideal daily amount and pattern of protein consumption for optimizing muscle health and improving metabolic functions of protein
4. Describe the synergistic effect on muscle protein synthesis of protein consumption combined with resistance exercise
5. State two strategies to counteract anabolic resistance in older adults
6. State two mechanisms by which intermittent fasting preserves muscle mass

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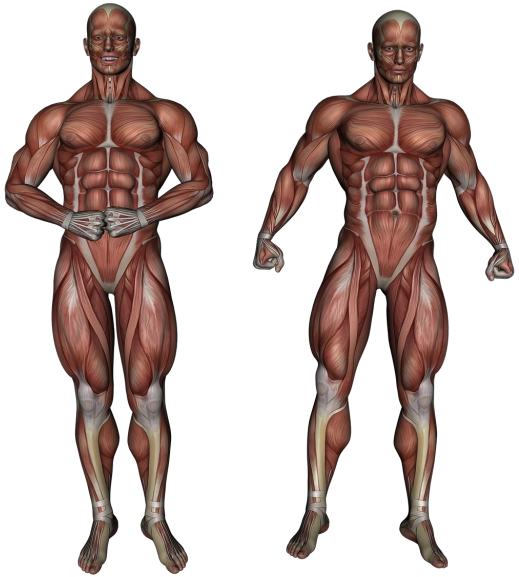

Part 1:

The Muscle-Disease Connection

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Sarcopenia

- Loss of muscle mass & muscle strength
  - Often but not exclusively seen in the aging
- Major determinant of impaired functionality in older adults
- Predominantly affects older adults & is correlated with disease
  - As early as 30 can progress gradually
  - Accelerates after 5th decade
- Can lead to ↓ QOL, loss of independence, need for long-term care, physical disability
- Exercise: most effective intervention

(Hoffmann & Weigert, 2017; Hunter G.R. et al., 2019; Jung HN et al., 2023; Mitchell W.K. et al., 2012; Robison et al., 2019)

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Osteosarcopenia

Osteosarcopenia: The comorbid disorders of sarcopenia & osteoporosis

- Characterized by infiltration of fat into muscle & bone
  - Both conditions linked to inadequate dietary protein
- Falls are the 2nd leading cause of unintentional injury death worldwide

(Hong & Kim, 2018; Hunter G.R. et al., 2019; World Health Organization, 2016)

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Bone Strength

- Bone is strengthened when voluntary forces (mechanical loading) are applied to the bone
- Bone cells (mainly osteocytes) sense high forces & respond by ↑ bone formation & bone density
- Maximum forces acting on bone are created by muscle
    - Those with sarcopenia have ↓ muscle mass & strength and weaker bones

(Hong & Kim, 2018; Hunter G.R. et al., 2019)

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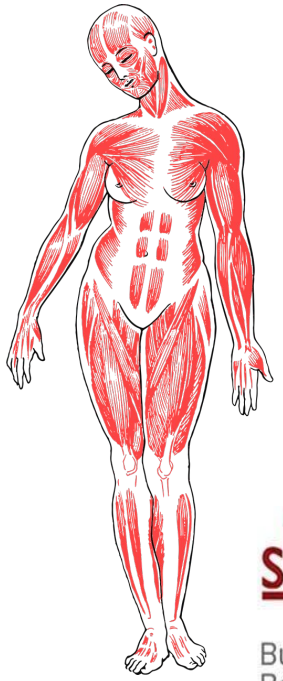
The Muscle-Disease Connection

Metabolic Function of Muscle are grouped into primary intersecting mechanisms of action:

1. Calorie burning
2. Blood sugar control
3. Metabolic flexibility
4. Excretion of myokines



(Stump C.S. et al., 2006)

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Muscle and Cardiorespiratory Fitness

Body composition is 1 of the 5 components of cardiorespiratory (aerobic) fitness

- Cardiorespiratory fitness (CRF) is a powerful indicator of overall health
  - Major risk factor for dying from CVD and from all causes
  - Strongly linked to mortality rates related to depression, dementia, & certain cancers (breast, colon/GI)
  - Measured by VO2max
    - Regular exercise ↑ VO2max & improves physical fitness

(Kaminsky L.A. et al., 2013)

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Muscle and Calorie Burning

- Muscle: major determinant of resting metabolic rate (RMR)
  - 20%-30% of RMR
  - RMR responsible for 60%-80% of total daily calories burned
- Muscle's contribution to ↑ energy expenditure is central to weight management

(Gim & Choi, 2016; Stump C.S et al., 2006)

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Poll Question

What percent of surplus glucose in the blood is taken up by muscle to be stored and used for energy?

a) 20%-30%
b) 40%-50%
c) 60%-70%
d) 80%-90%

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Muscle and Blood Sugar Control

- Muscle takes up & stores 80%-90% of surplus glucose in the blood & uses it for energy
  - Facilitated by signaling action of insulin → induces glucose transporter GLUT4 to enable glucose to enter cell
- ↑ muscle mass above even average levels is shown to ↑ insulin sensitivity & glucose uptake from the blood
  - Muscle enhancement associated with 63% ↓ in DM prevalence
  - Muscle mass loss ↑ risk of insulin resistance
  - Exercise → long-standing improvement in muscle insulin sensitivity & glu regulation

(Chadt & Al-Hasani, 2020; Kirwan J.P. et al., 2017; Srikanthan & Karlamangla, 2011)

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Muscle Mass Loss and Blood Sugar

↑ BS resulting from muscle loss can ignite chronic inflammation → further ↓ muscle mass & strength

- Serum glucose & insulin ↑ with age as ability to properly metabolize glucose progressively deteriorates
- Hyperglycemia → oxidative stress & inflammation
  - ↑ ROS & suppresses antioxidant defense system
  - AGEs accumulation

(Ferrucci & Fabbri, 2018; Fournet M. et al., 2018; Oguntibeju, O.O., 2019; Singh & Newman, 2011)

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Muscle and Metabolic Flexibility

Metabolic flexibility: ability to periodically transition freely between 2 primary fuels (glucose & fat) depending on supply & demand

- Muscle can utilize fat or glucose as its main fuel
- Historically allowed humans to withstand extreme fluctuations in fuel supply
- Sedentary & obese individuals → compromised metabolic flexibility
    - muscle less able to clear away glu after eating
    - ↓ ability to burn stored fat while fasting
    - contributes to TG accumulation within muscle cells → interferes with insulin signaling

(Anton S.D. et al., 2018; Kelley D.E., 2005; Kelley & Mandarino, 2000)

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Muscle and Myokine Excretion

Myokines: signaling molecules (hormones) produced by muscle

- Interleukin 6 (IL-6)
  - ↑ BS control, ↓ body fat & fat within muscle fibers, anti-inflammatory effects, tumor growth suppression, appetite inhibition, ↑ muscle mass/strength in response to RT
- Myostatin
  - Impairs muscle synthesis & promotes muscle breakdown, ↑ fat mass
- Brain-derived neurotrophic factor (BDNF)
  - Strengthens synaptic plasticity fundamental for learning & memory

(Leal L.G. et al., 2018; Severinsen & Pedersen, 2020; Sleiman S.F. et al., 2016)

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Part 2:

Muscle Protein Synthesis and Muscle Maintenance

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Muscle Protein Synthesis (MPS)

Occurs when dietary proteins are broken down via digestion to essential amino acids (AAs) → assemble new proteins that are taken up by muscle tissue

Major Triggers

1. Resistance exercise
2. Amino acids (only mandatory trigger)
3. Insulin

Building muscle is ~75% exercise, ~25% protein

(Bell K.E. et al., 2016)

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Physical Inactivity and Insulin Resistance

- Physical inactivity is a major promoter of insulin resistance & sarcopenia
- Long-term muscle disuse from chronic inactivity & recurrent periods of muscle disuse ↓ sensitivity of muscle to the anabolic stimulation of AAs & insulin → *anabolic resistance*
  - May contribute to loss of muscle mass, strength, & functionality
- Physical inactivity can ↑ systemic inflammation & oxidative stress
  - Key contributors to insulin resistance

(Bell K.E. et al., 2016; Lawler & Hindle, 2011)

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Exercise Benefits

- Restores capacity of muscle mitochondria to burn fat
  - Possibly through ↑ gene expression targeting fat burning in muscle & mitochondrial biogenesis
  - Associated with improved metabolic flexibility & ↓ risk of metabolic diseases
- Most effective intervention for sarcopenia
- Aerobic & RT cause a reduction in myostatin to prevent muscle loss

(Berggren J.R. et al., 2012; Hoffmann & Weigert, 2017; Schnyder & Handschin, 2015; Yang X. et al., 2019)

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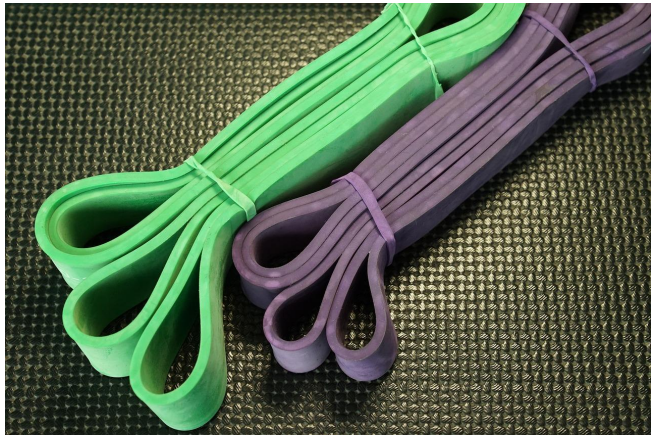
Resistance Training

- Predominant type of exercise for developing optimal muscle mass, strength, & muscle quality
  - Weightlifting, elastic bands, wt machines, medicine balls, body wt, kettlebells
- Targets type II (fast-twitch) muscle fibers that atrophy with age
  - Type I (slow-twitch) generally do not atrophy
- Goal: perform with high intensity of effort sufficient to reach muscle fatigue at end of set
- Only 9% of people >75 perform strength training regularly
- Even nonagenarians can achieve gains in muscle mass & strength



(Damas F. et al., 2016; Fiatarone M.A. et al., 1990; Jensen J. et al., 2011; Ogborn & Schoenfeld, 2014; Phillips & Winett, 2010)

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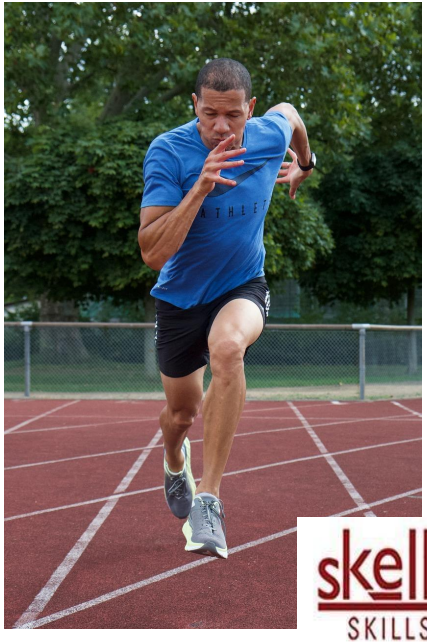
High-Intensity Interval Training (HIIT)

- Time-efficient alternative to steady-state cardio
- Brief, intermittent burst of vigorous effort (5 sec to 8 min at 80-90% of maximal HR) interspersed with recovery periods of rest or lower-intensity exercise - performed for 3 to 4 cycles
- Studies show HIIT is more effective than moderate-intensity steady-state cardio for ↑ cardiorespiratory fitness
- Shown to active muscle satellite (stem) cells & drive MPS when paired with high-quality dietary pro
- Improves muscle strength & power
    - Muscle power = strength + speed, or ability to exert a force quickly



(Callahan M.J. et al., 2021; Medicine, A.A.C.o.S., 2014; Ramos J.S. et al., 2015)

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Optimal Daily Protein Intake

- 1.2 g/kg body weight/day to 1.8 g/kg body weight/day
  - This doubles the RDA, which was determined from nitrogen balance studies of subjects mostly in their 20s & 30s
- Higher pro intakes of > 1.2 g/kg body wt daily suggested for older adults who exercise & are otherwise active (for growth & muscle maintenance)
- By appx age 30, anabolic effects of growth hormones (insulin, growth factor, IGF-1, steroid hormones) pronounced in children & young adults begin to significantly ↓

(Bauer J. et al., 2013; Hevia-Larrain V. et al., 2021; Rand W.M. et al., 2003)

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Protein and MPS Regulation

- Mammalian target of rapamycin (mTOR): master regulator of MPS & muscle hypertrophy
  - Responds to nutritional & environmental cues
- Adequate nutrients & AAs: activates mTOR → drives anabolic processes, shuts down catabolic processes
  - ↑ Cell growth, protein synthesis
  - Halts autophagy
    - Eliminates cellular waste & maintains cell repair & function
    - Preserves & ↑ muscle mass by removing damaged muscle fibers/ regenerating new muscle fibers
    - Muscle autophagy declines with age

(Layman D.K. et al., 2015; Li S. et al., 2017; Park S.S. et al., 2019; Saxton & Sabatini, 2017)

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Poll Question

Approximately how many grams of protein should be consumed at each meal in order to optimize muscle health and improve metabolic function?

a) 10-30 grams
b) 30-50 grams
c) 50-70 grams
d) 70-90 grams

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Protein and Meal Thresholds

- Quantity & quality of protein (AAs) consumed during meals matters
- 30-50 g pro (4-6 oz) at each of the 3 daily meals provides 3g leucine & is ideal for optimizing muscle health & improving metabolic functions of protein
    - 3g leucine at meals can help to overcome anabolic resistance in vegans & older adults
    - Clinical trials indicate that meals containing > 2.2 g leucine are required to activate mTOR signaling & MPS
    - 30 g of high-quality Pro per meal provides appx 2.5 g leucine
- Space meals 3-5 hours apart

(Bauer J. et al., 2013; Layman D.K., 2009; Moore D.R. et al., 2015; Morton R. et al., 2018; Phillips S.M. et al., 2020; Stokes T. et al., 2018; Yoon M.S., 2017)

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Protein Intake and Resistance Training (RT)

- Causes a synergistic effect on MPS
- RT ↓ threshold at which dietary pro activates mTOR → drives muscle growth
    - Heightened sensitivity of muscle to anabolic effects of pro for at least 24 hrs after a workout
- In adults, the greatest muscle benefits are achieved when a meal rich in protein is consumed after exercise
    - Ideal to consume 20-40 g high-quality animal protein to maximize MPS
        - Provides 1.8-4 g leucine

(Layman D.K. et al., 2015; Reidy & Rasmussen, 2016)

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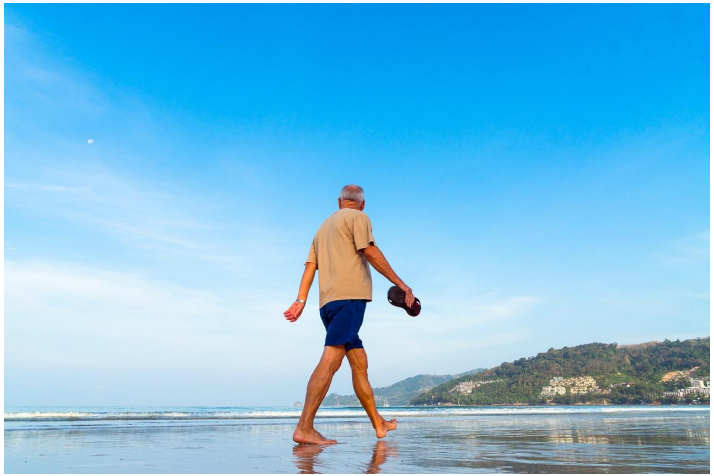
Anabolic Resistance in Older Adults

- Aging muscle is less responsive to muscle-building triggers than young muscle
- Anabolic resistance can lead to negative net pro balance → muscle pro breakdown exceeds MPS
  - Can result in muscle atrophy & is a major driver of sarcopenia
- Causes:
  - Chronic inactivity → ↓ MPS, causes excessive autophagy → muscle loss
  - Abnormally ↑ activation of mTOR in the fasting state → muscle atrophy



(Barclay R.D. et al., 2019; Bauer J. et al., 2013; Beals J.W., 2019; Layman D.K. et al., 2015; Marshall R.N. et al., 2020)

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Counteracting Anabolic Resistance

1. Diet:
    a. ↑ Pro amplifies the anabolic signal to construct muscle protein
2. Exercise:
    a. Exercise, esp RT, ↑ muscle sensitivity to anabolic stimuli (leucine)
    b. Best to consume high-quality pro after RT
    c. Recc: RT 3x/wk

(Beals J.W., et al., 2016; Drummond M. J. et al., 2008; Moore, D.R., et al., 2015)

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Protein Needs in Older Adults

- Require higher intakes of post-exercise pro to maximize anabolic response to training
- Amount of dietary pro relative to lean body mass (body wt excluding fat) needed by older adults to maximize MPS is appx 140% more protein than what's required by younger individuals
- During at least 2 meals 30-50 g high-quality pro providing at least 3 g of leucine should be consumed
    - Offsets anabolic resistance

(Moore, D.R., et al., 2015; Morton, R., et al., 2018)

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Part 3:

Nutrition and Lifestyle Approaches for Maximizing Muscle and Health

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Low-Carbohydrate

- Studies indicate low-carb, higher-protein may be more effective for maintaining muscle mass & improving body composition
  - Improves cardiovascular risk factors
  - T2D management
  - Protects against CA, AD, PD
  - 30-50 g pro 3x/day
- Insulin resistance contributes to age-related muscle loss
  - Chronic high-carb diet → muscle insulin resistance → contributes to sarcopenia
  - Chronic high-carb diet → chronic mTOR activation → poor muscle health
- Goal carb intake 25%-40% of total calories

(Devkota & layman, 2011; Elisia & Krystal, 2021; Lopez Teros M.T. et al., 2015; Szypowska & Regulska-Ilow, 2019; Wlodarek D., 2019)

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Leucine

- Branched-chain amino acid (BCAA)
- Primary AA that drives mTOR & MPS
  - Independently activates mTOR, even at rest
- Whey protein: ~12% leucine
- Grain proteins: ~6% leucine

(Gran & Cameron-Smith, 2011; Phillips S.M. et al., 2020)

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Intermittent Fasting (IF)

- Time-restricted feeding (TRF): one of most popular & well-tolerated IF methods
  - Ex: restrict eating window to 6-8 hours to allow for a 16-18 hour fast
- Can help to counteract chronicity of mTOR & insulin activity d/t high-carb diet
- “Hormesis”: a mild “good” stress elicits adaptive beneficial response that ↑ resilience
  - Greater metabolic flexibility

(Mattson M.V. et al., 2017; Longo & Mattson, 2014; Patterson R.E. et al., 2015)

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IF and Muscle Mass Preservation

IF preserves muscle mass through:

- **Autophagy activation**
- **Flipping the 'metabolic switch'** from burning glu to fat & fat-derived ketones in muscle mitochondria
  - fewer mitochondrial free radicals generated when fat & ketones are burned for fuel
  - destruction/elimination of defective mitochondria in muscle cells (major contributors to muscle loss)
  - ↑ mitochondrial biogenesis, improved mitochondrial function
- **Enhanced (GH) secretion** → suppresses muscle protein breakdown
- **Muscle cells are not among the first cells to be broken down** for glu during a fast (high turnover cells are utilized first - gut, skin cells)

(Anton S.D. et al., 2018; Bhutani S. et al., 2013; Martinez-Lopez, N. et al., 2017; Moro T. et al., 2016; Vendelbo, M. H. et al., 2010)

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Counseling Clients on IF

- A ketogenic diet for a few weeks preceding a fast can prepare the body for IF
  - Enable the body to 'flip the metabolic switch' and burn fat (& ketones) more readily for energy
    - Avoid carb/sugar cravings & dips in BS
    - Make it easier to transition to fasting
- Wt loss from short-term IF (TRF< ADF) spares lean muscle mass
  - Retention of lean mass during IF shown to be improved by endurance & resistance exercises
- Exercising while fasting enhances muscle glycogen depletion → MPS & muscle growth
  - Fasting depletes liver glycogen, generating ketones, which preserve muscle
- Contraindicated for some groups
  - Children, breastfeeding/pregnant women, underweight, elderly

(Anton S.D. et al., 2018; Bhutani S. et al., 2013; Grajower & Horne, 2019; Martinez-Lopez, N. et al., 2017; Moro T. et al., 2016)

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Post-Workout Protein

- Young adults: 5-20 g to activate MPS beyond exercise alone
- Ideal to consume within 2 hours of exercise completion
    - Reverses catabolism in physically inactive/untrained individuals
    - Enhances exercise-induced mTOR & MPS activation in untrained individuals
- RT in a Fasted state: consume high-quality pro immediately after exercising
- Consuming before a workout (not > 3-4 hrs) enables AA delivery to muscle that's sustained into the recovery period & makes immediate post-exercise pro intake less necessary
- Whey protein
    - Rapid digestion
        - Rich leucine content

(Aragon & Schoenfeld, 2013; Devries & Phillips, 2015; Reidy & Rasmussen, 2016)

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Creatine

- One of most researched sports supplements
- Compound of methionine, arginine, & glycine
- ½ is made in the body, ½ is obtained from seafood, meat, & poultry & stored in muscle
- Linked with phosphorus to form phosphocreatine → donates the phosphorus to ADP to regenerate ATP
- Most beneficial for brief, all-out exertion lasting up to 6 sec
    - Weightlifting, sprinting
- When combined with RT, ↑ muscle mass, strength, & power
- May counteract age-related muscle loss in older adults, even without RT

(Candow D.G. et al., 2019; Smith R.N. et al., 2019)

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Questions?

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More On This Topic

Thank you for attending!

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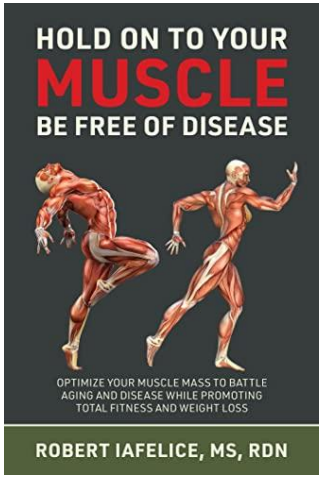
- *A Practitioner's Guide to Intermittent Fasting: Evidence, Analysis and Real-World Insight*
- *Peak: The New Science of Athletic Performance That is Revolutionizing Sports*



- Live attendees: You'll get a link to the feedback survey in one hour/CE Cert tomorrow

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