Supplemental Protein in Support of Muscle Mass and Health: Advantage Whey

Michaela C. Devries and Stuart M. Phillips

Abstract: Skeletal muscle is an integral body tissue playing key roles in strength, performance, physical function, and metabolic regulation. It is essential for athletes to ensure that they have optimal amounts of muscle mass to ensure peak performance in their given sport. However, the role of maintaining muscle mass during weight loss and as we age is an emerging concept, having implications in chronic disease prevention, functional capacity, and quality of life. Higher-protein diets have been shown to: (1) promote gains in muscle mass, especially when paired with resistance training; (2) spare muscle mass loss during caloric restriction; and (3) attenuate the natural loss of muscle mass that accompanies aging. Protein quality is important to the gain and maintenance of muscle mass. Protein quality is a function of protein digestibility, amino acid content, and the resulting amino acid availability to support metabolic function. Whey protein is one of the highest-quality proteins given its amino acid content (high essential, branched-chain, and leucine amino acid content) and rapid digestibility. Consumption of whey protein has a robust ability to stimulate muscle protein synthesis. In fact, whey protein has been found to stimulate muscle protein synthesis to a greater degree than other proteins such as casein and soy. This review examines the existing data supporting the role for protein consumption, with an emphasis on whey protein, in the regulation of muscle mass and body composition in response to resistance training, caloric restriction, and aging.

Keywords: caloric restriction, hypertrophy, muscle, protein, sarcopenia, whey

Introduction

Skeletal muscle mass is an integral body tissue playing key roles in strength, performance (both in sport and activities of daily living), and metabolic regulation. As we grow there is a corresponding increase in skeletal muscle mass; however, once growth is complete there is usually no net increase in muscle mass. Moreover, starting as early as the 4th decade of life skeletal muscle mass naturally starts to decline at a rate of approximately 0.8% per year, a process termed sarcopenia (Paddon-Jones and Rasmussen 2009). Given the instrumental role of muscle in locomotion, force production, glucose disposal (DeFronzo and others 1992), and metabolic regulation (Karagounis and Hawley 2010), the loss, or low levels, of muscle mass increases the risk of chronic diseases such as metabolic syndrome, type II diabetes, and cardiovascular disease (Jurca and others 2005; Wolfe 2006), as well as falls (Landi and others 2012; Scott and others 2014) and ability to perform activities of daily living (Velazquez Alva Mdel and others 2013; da Silva Alexandre and others 2014), all of which decrease quality of life. As such, optimizing muscle mass across the lifespan for optimal performance and overall health is of utmost importance.

Skeletal muscle mass is the product of continuous and simultaneous processes of muscle protein synthesis (MPS) and muscle protein breakdown (MPB) and it is the net balance between these 2 processes that determine whether muscle mass increases (positive protein balance), decreases (negative protein balance), or remains constant. In healthy individuals between the ages of 20 and somewhere into their mid-to-late thirties, MPS usually equals MPB and muscle mass does not change. However, when MPS predominates an increase in muscle mass occurs, such as when weights are lifted, termed muscle hypertrophy; whereas when MPB predominates a decrease in muscle mass occurs, termed muscle atrophy when immobilization is present (such as during casting for fractured limbs) or sarcopenia when it is an insipid age-related process.

Over the course of a day, rates of MPS and MPB continuously fluctuate (Figure 1, upper panel). Following the consumption of a protein-containing meal, short-term periods of hyperaminoacidemia stimulates MPS and hyperinsulinemia inhibits MPB resulting in net positive protein balance. As time after a meal increases, rates of MPS decrease and MPB increase and protein balance switches to negative until a subsequent meal is consumed. In healthy, nonexercising individuals in energy balance these periods of net positive and negative protein balance are equal and muscle mass remains constant (Figure 1A). However, the ratio of MPS and MPB can be influenced by several factors including energy deficit, resistance training, and aging. It is well known that resistance exercise stimulates both MPS and MPB (Figure 1B), and that if a protein-containing meal is consumed in close proximity to the exercise bout, net positive protein balance ensues (Figure 1C) (Tipton and others 2007; Wilkinson and others 2007), resulting in muscle hypertrophy over time (Esmarck and others 2001; Hartman and others 2007; Cermak

MS 20141503 Submitted 9/5/2014, Accepted 12/1/2014. *Authors are with Exercise Metabolism Research Group (EMRG), Dept. of Kinesiology, McMaster Univ., 1280 Main St. W, IWC E210, Hamilton, ON, L8S 4K1, Canada. Direct inquiries to author Phillips (E-mail: phillis@mcmaster.ca).*

Author disclosures: SMP has research sponsored by the Whey Protein Consortium through the Dairy Research Institute (DRI). In addition, SMP has given talks on behalf of the DRI and received cost of living expenses for those talks.

doi: 10.1111/1750-3841.12802

Journal of Food Science A Publication of the Institute of Food Technologists

and others 2012). On the other hand, rates of MPS are lower and net negative protein balance ensues during periods of energy deficit (Pasiakos and others 2010; Areta and others 2014) and with increasing age (Figure 1D) (Volpi and others 2000; Cuthbertson and others 2005; Phillips 2009), resulting in muscle mass loss. However, it has now been established that this loss of muscle mass during energy deficit and with aging can be attenuated by the consumption of a higher-protein diet (Houston and others 2008; Josse and others 2011; Wycherley and others 2012; Geirsdottir and others 2013).

Protein-containing foods include animal sources such as meat, fish, dairy products, and eggs and vegetarian sources such as tofu, legumes, and quinoa. Of note, the proteins in dairy products such as milk, yogurt, and cheese are of the highest quality and their consumption following a bout of resistance exercise (Wilkinson and others 2007), during a period of resistance training (Hartman and others 2007) and during caloric restriction (Josse and others 2011) result in a greater positive protein balance than that seen with other protein sources. The 2 proteins in milk are casein (about 80% of protein content) and whey (about 20% of protein content). Whey is a "by-product" of cheese production (or can be specifically isolated through a complicated filtration of milk) and its protein is one of the most commonly used supplements by athletes and sports nutrition product consumers to support muscle hypertrophy and improve body composition. The purpose of this review is to examine the existing data supporting a role for protein consumption, in particular whey protein, in the regulation of muscle mass and body composition across the adult lifespan.

Whey Protein: Why Is It Superior to Other Proteins to Stimulate MPS?

Whey protein has been shown to stimulate MPS to a greater extent than casein and soy protein at rest and following exercise in young and older individuals (Tang and others 2009; Pennings and others 2011; Burd and others 2012; Yang and others 2012b). The differential MPS response to protein feeding is a function of the quality of the ingested protein. Proteins differ in their quality based on their amino acid (AA) content, digestibility, and bioavailability (FAO/WHO Expert Consultation 1991). Upon ingestion whey protein is rapidly digested and, since it is acid-soluble, it exits the stomach rapidly resulting in a pronounced rise in blood AA, which is thought to be critical to the stimulation of MPS (Katsanos and others 2006; Dreyer and others 2008; Tang and others 2009; West and others 2011). In comparison to other supplemental proteins, whey and soy proteins are considered to be "fast"-digested proteins, while casein is considered to be a "slow"-digested protein as it clots due to the acid pH of the stomach and exits slowly into the small intestine (Boirie and others 1997; Bos and others 2003). Of importance is that whey protein is a complete protein, meaning it contains all of the essential amino acids (EAAs), and has a high proportion of the branched-chain AA (BCAA) leucine, a key AA in the stimulation of the MPS (Anthony and others 2001). In fact, while both soy and casein are also complete proteins, whey protein has greater EAA and leucine contents than casein, soy, and collagen proteins. In addition to having a lower leucine content, the bioavailability of amino acids from soy protein to support MPS is inferior to

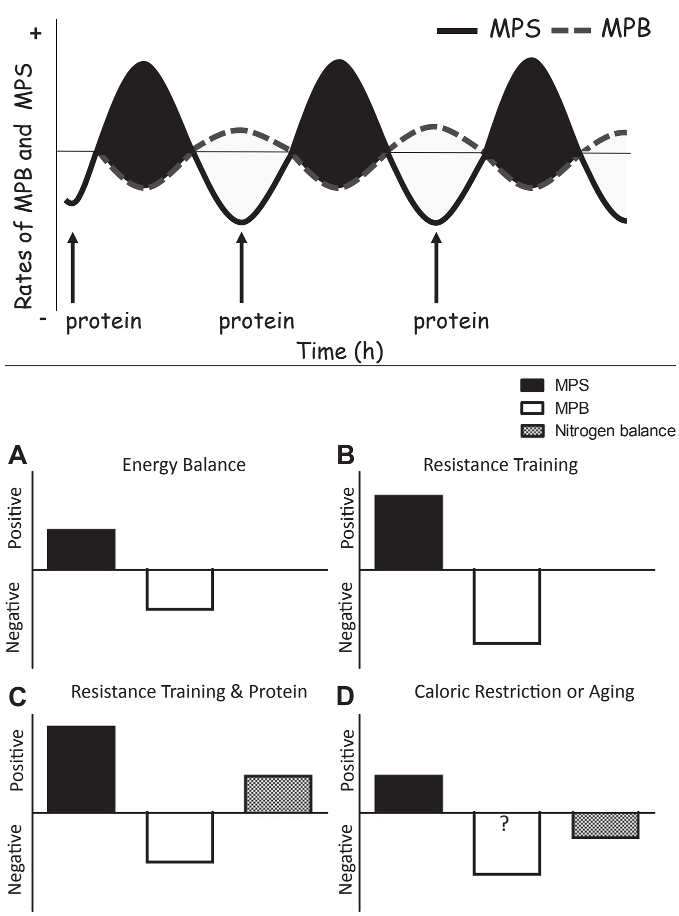

Figure 1–Upper: Fluctuating rates of MPS and MPB over the course of the day. When protein is consumed there is an increase in rates of MPS and a decrease in rates of MPB resulting in net positive nitrogen balance (MPS > MPB, black areas). A few hours after the meal rates of MPB increase and MPS decrease resulting in net negative nitrogen balance (MPS < MPB, white areas). In healthy individuals in energy balance the total AUC of positive and negative nitrogen balance are equal over the course of the day (MPS = MPB; AUC black = AUC white) and muscle mass is maintained (Tang and Phillips 2009). Lower: Representation of overall 24-h MPS (black), MPB (white), and Net Balance (hatched) in different conditions. (A) Healthy individual in energy balance resulting in nitrogen balance and maintenance of muscle mass over time; (B) independent effect of resistance training alone (that is, absence of postworkout nutrition) to increase both MPS and MPB resulting in nitrogen balance and maintenance of muscle mass over time (Phillips and others 1997); (C) synergistic effect of resistance training and postexercise protein consumption to further heighten MPS and abolish the increase in MPB resulting in positive nitrogen balance and muscle gain over time (Wilkinson and others 2007); (D) aging and caloric restriction both decrease MPS; however, their effect on MPB is controversial (increase or no change—as denoted by "?" in the figure) yet overall they both result in negative nitrogen balance and muscle loss over time (Phillips 2009; Areta and others 2014).

Table 1–Protein quality characteristics of commonly used protein supplements.

	Whey	Casein	Soy	Hydrolyzed collagen
Complete protein?	Yes	Yes	Yes	No
Digestibility	Fast	Slow	Fast	Fast
Amino acid content (g/25 g protein)				
Leucine	3.0	2.3	1.5	0.8
Σ EAA	12.4	11.0	9.0	3.8
Σ BCAA	5.6	4.9	3.4	1.4
Splanchnic AA extraction	Low	Low	High	High
PDCAAS	1.0	1.0	1.0	0.0

AA, amino acid; BCAA, branched-chain amino acid; EAA, essential amino acid; PDCAAS, protein digestibility corrected amino acid score. References for information contained in Table 1: Whether a protein is a complete protein and its specific amino acid content can be found in the USDA National Nutrient Database for Standard Reference—http://ndb.nal.usda.gov/ (United States Dept. of Agriculture). All proteins other than casein are considered fast proteins. The rapid rise with soy and whey ingestion, as compared with the slow rise with casein ingestion, in plasma amino acid concentration is shown by Tang and others (2009). The splanchnic extraction of a protein is based on its amino acid content. The BCAA undergo less splanchnic extraction and thus proteins with higher BCAA content have more amino acids available to support muscle protein synthesis (Fouillet and others 2002; Luiking and others 2005). Lastly, the FAO/WHO expert consultation report on protein quality provides the PDCAAS equation to determine the PDCAAS for any protein (FAO/WHO Expert Consultation 1991). Of note, only complete proteins will have a PDCAAS greater than 0.0. Proteins with a PDCAAS >1.0 have their scores truncated at 1.0.

that of whey and casein, with a greater amount being directed toward splanchnic catabolic activity and urea synthesis (Luiking and others 2005; Fouillet and others 2009) as well as oxidation (Yang and others 2012b). In addition, the higher BCAAs, particularly leucine, found in milk, as compared with soy, are readily available to peripheral tissues and are able to support MPS (Fouillet and others 2002). The differences in protein quality characteristics between whey, casein, soy, and collagen proteins are summarized in Table 1. Together, the differences in digestibility, AA content, and AA bioavailability result in a significantly lower rise in blood leucine and blood EAA concentration following consumption of isoenergetic, isonitrogenous casein, and soy (and presumably collagen) beverages, as compared with whey (Tang and others 2009; Burd and others 2012).

The importance of leucine to stimulate MPS is underscored by numerous animal and human trials showing that administration of leucine can stimulate MPS (Anthony and others 2000; Crozier and others 2005; Escobar and others 2006; Katsanos and others 2006), which has given rise to the concept of the leucine threshold (Figure 2). The leucine threshold (or leucine "trigger") hypothesis states that in order for a robust increase in MPS to ensue following protein consumption, the muscle intracellular leucine concentration needs to reach a given level—the leucine threshold (Phillips 2014). Importantly, this threshold can be manipulated, being lowered by factors such as resistance training and being increased by factors such as aging and physical inactivity (Moore and others 2014; Witard and others 2014). Given the fluctuating nature of this threshold, the exact amount of leucine that needs to be consumed to exceed the threshold has yet to be established and will vary within a population based on age and physical activity level. Our lab (Moore and others 2009) and others (Witard and others 2014) have found that 20 g of high quality protein, containing 1.7 to 2.4 g of leucine, maximally stimulates MPS, a level which likely represents the absolute minimum amount of leucine needed to be consumed given that the subjects tested were resistance trained young men. Furthermore, given the leucine threshold, whether the addition of leucine to a suboptimal dose of protein can enhance its anabolic ability has also been examined. In particular, our laboratory has previously shown that the addition of 5 g, but not 3 g, leucine to 6.25 g of whey protein isolate stimulated MPS to the same extent as an optimal (25 g) dose of whey protein isolate (Churchward-Venne and others 2014). Furthermore, the addition of leucine to a protein/carbohydrate beverage resulted in a greater increase in MPS than a protein/carbohydrate beverage alone following a bout of resistance exercise (Koopman and others 2005), indicating that leucine can enhance the anabolic effect of protein. Of importance, while leucine can independently stimulate MPS (Anthony and others 2000; Crozier and others 2005; Escobar and others 2006; Katsanos and others 2006), in the absence of EAA MPS would be limited. As such, given the role of leucine in the stimulation of MPS and that whey protein is an excellent source of leucine, BCAAs, and EAAs and is rapidly digested, whey protein is an excellent protein source for the stimulation of MPS and thus the regulation of muscle mass across the lifespan.

The Role for Whey Protein to Promote Muscle Hypertrophy with Resistance Exercise

Numerous trials have shown that the consumption of protein following a bout of resistance exercise increases MPS (Tipton and others 2004; Wilkinson and others 2007; Tang and others 2009; West and others 2011; Burd and others 2012) in a dose-dependent manner (Moore and others 2009; Pennings and others 2012; Yang and others 2012a, 2012b; Witard and others 2014). Resistance exercise alone stimulates MPS, but it also increases MPB, resulting in a net loss of muscle protein in the absence of an increase in amino acid availability (Phillips and others 1997). With the provision of protein following a bout of resistance exercise there is a synergistic effect of resistance exercise and protein, resulting in a greater increase in MPS than either stimulus would induce

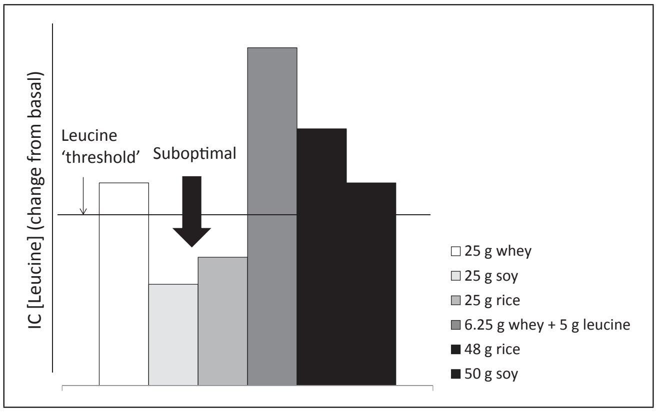

Figure 2–Intracellular (IC) leucine concentration achieved following the consumption of various doses of protein in relation to the leucine "threshold." Of importance, this figure has been generated based on data from young, resistance-trained subjects. The leucine threshold increases with increasing age and physical inactivity. After ingestion of 25 g of whey protein the IC [leucine] exceeds the leucine threshold and a robust MPS response is observed. In comparison, following consumption of 25 g of soy or rice protein IC [leucine] concentration does not reach the leucine threshold and the MPS response is blunted. However, protein can be manipulated by (1) increasing the dose to ensure it provides enough leucine to reach the leucine threshold (for example, 48 g of rice protein or 50 g of soy protein) or (2) by adding leucine to a suboptimal dose of protein (for example, 6.25 g whey + 5 g leucine), which would result in a robust MPS response. Still, it is important to note that increasing the amount of protein consumed in order to achieve a leucine intake that exceeds the leucine threshold would also increase the amount of calories consumed (for example, 25 g of whey protein isolate = 100 kcal compared with 200 kcal for 50 g soy protein and 240 kcal for 48 g rice protein), which is not ideal for those looking to restrict energy intake or for older adults who have lower appetites.

alone, and completely abolishing the increase in MPB (Biolo and others 1997; Tang and others 2009; Burd and others 2012; Yang and others 2012a, 2012b), which over time will lead to muscle hypertrophy (Hartman and others 2007; Cermak and others 2012; Tieland and others 2012a). In fact, a recent meta-analysis of randomized controlled trials found that dietary protein supplementation during resistance training (> 6 wk) resulted in greater gains in lean body mass and strength in younger and older adults (Cermak and others 2012).

The timing of protein intake following a bout of resistance exercise is also an important consideration. Consuming a protein supplement during what is termed the "anabolic window" (<1 h before or after resistance exercise) is thought to be ideal for promoting muscle hypertrophy and strength gains with resistance training (Volek 2004; Stark and others 2012). Several studies have shown that when protein is consumed in the time period before and/or after resistance exercise there are greater gains in muscle mass (Esmarck and others 2001; Andersen and others 2005; Bird and others 2006; Candow and others 2006; Hartman and others 2007; Hulmi and others 2009; Josse and others 2011) and strength/performance (Andersen and others 2005; Bird and others 2006; Candow and others 2006; Coburn and others 2006; Josse and others 2011), as compared with placebo, following a period of resistance training. However, not all trials have found that protein consumption in the peri-workout period influences muscle hypertrophy or strength with resistance training (Hoffman and others 2009; Verdijk and others 2009; Wycherley and others 2010). In fact, while a recent meta-analysis showed that protein consumed during the so-called "anabolic window" resulted in greater muscle hypertrophy following a period of resistance training, when adjusted for total daily protein intake the effect of protein timing on muscle hypertrophy disappeared (Schoenfeld and others 2013). In addition, timing of protein intake did not result in greater strength gains following resistance training (Schoenfeld and others 2013). As such it seems as if absolute daily protein intake, not timing of protein intake, is the greatest predictor of muscle hypertrophy following resistance exercise. However, an important consideration is that adequate protein is consumed during the day to allow for maximal muscle hypertrophy, which would more than likely naturally result in consumption of protein in the hours before and/or after a resistance exercise bout.

Numerous studies have shown that milk is superior to other protein sources in stimulating MPS at rest (Tang and others 2009; Pennings and others 2011; Burd and others 2012; Yang and others 2012b) and following an acute bout of resistance exercise (Wilkinson and others 2007; Tang and others 2009; Burd and others 2012; Yang and others 2012b), as well as in promoting greater muscle hypertrophy and strength gains following a period of resistance training (Cribb and others 2006; Hartman and others 2007; Volek and others 2013). Additionally, studies have found that it is the whey protein fraction of milk that is responsible for the greater increase in MPS as whey induces a greater MPS response than casein when consumed at rest and following exercise (Tang and others 2009; Pennings and others 2011; Burd and others 2012). As detailed above, this greater increase in MPS is the result of rapidly induced hyperaminoacidemia and hyperleucinemia that follows whey consumption (Tang and others 2009). Specifically, our lab has shown that by manipulating the ingestion of whey protein (25 g bolus compared with 10×2.5 g pulses every 20 min) the rapid rise in plasma amino acids and leucine induced by bolus whey ingestion resulted in greater rates of MPS after a bout of resistance exercise as compared with pulsed whey ingestion (West and others 2011). Importantly, this occurred despite nearly identical net EAA and leucine exposure (West and others 2011). These findings highlight the importance of rapid hyperaminoacidemia, and particularly rapid hyperleucinemia, in the optimal stimulation of MPS.

We have previously shown that acute changes in MPS induced by protein consumption after resistance exercise (Wilkinson and others 2007) can predict long-term changes in body composition in response to protein feeding during resistance training (Hartman and others 2007). Specifically, we have shown that the MPS response following an acute bout of resistance exercise is greater with milk (18 g protein) as compared with soy (18 g protein) (Wilkinson and others 2007). These results translated to greater gains in lean mass, type I and II muscle fiber cross-sectional area, and greater losses of fat mass with postexercise milk (35 g protein) as compared with soy (35 g protein) consumption during 12 wk of resistance training in untrained young men, with no difference in strength gains (Hartman and others 2007). Similarly, Volek and others (2013) found greater gains in lean body mass with whey protein (about 22 g/d) consumption during a 9-mo supplementation and resistance training intervention as compared with soy (about 22 g/d). In addition, whey protein increased fasting plasma leucine concentration to a greater extent than soy supplementation, and fasting leucine concentrations were positively correlated with changes in lean body mass (Volek and others 2013), again highlighting the importance of leucine in stimulating MPS and inducing muscle hypertrophy. Likewise, Cribb and others (2006) found that whey induced a greater increase in lean body mass and a greater decrease in fat mass, as compared with casein, during a 10-wk resistance training protocol in resistance-trained men. Furthermore, whey induced greater increases in strength as compared with casein consumption during resistance training, even when expressed relative to body weight (BW) (Cribb and others 2006). However, not all trials have found whey to be superior to soy (Candow and others 2006; DeNysschen and others 2009) or rice protein (Joy and others 2013) in promoting muscle hypertrophy with resistance training. In a study by Joy and others (2013) subjects were randomized to consume either 48 g of rice or whey protein isolate immediately postexercise during an 8-wk progressive, nonlinear resistance-training protocol. While lean body mass, muscle thickness, and strength increased, there were no differences between groups. The authors acknowledged that this finding was likely due to the high dose of protein (48 g) used in the study, which provided 5.5 and 3.8 g of leucine in the whey and rice drinks, respectively, which are both greater than the 2.0 to 3.5 g of leucine that has been proposed to be the range of leucine intake where MPS is maximally stimulated (Moore and others 2009). In addition, all subjects were put on a diet consisting of 25% protein throughout the intervention and thus habitual daily protein intake might have already saturated the MPS response. In the 2 studies that did not find a difference in lean mass or strength gains between whey- and soy-supplemented groups following resistance training the habitual diet of the subjects contained 1.2 g and 1.6 to 1.9 g/kg/day protein without the inclusion of the supplement and thus might have been providing enough protein throughout the day and immediately postexercise to maximally stimulate MPS and induce equal increases in strength and muscle hypertrophy (Candow and others 2006; DeNysschen and others 2009). On balance, we view the available evidence as being strongly suggestive that whey protein is superior to other protein types in stimulating MPS following a bout of resistance exercise and inducing muscle hypertrophy with resistance training.

Optimizing Protein Consumption to Attenuate Muscle Mass Loss While Aging

The progressive loss of muscle mass and strength, sarcopenia, that accompanies aging can make it more difficult to perform activities of daily living (Velazquez Alva Mdel and others 2013; da Silva Alexandre and others 2014) and increases risk of falls (Landi and others 2012; Scott and others 2014), thus impacting quality of life. In addition, as skeletal muscle is the largest site of blood glucose disposal (DeFronzo and others 1992), the loss of muscle mass can lead to increased risk for metabolic syndrome, diabetes, and premature mortality (Jurca and others 2005; Wolfe 2006; Ruiz and others 2008). As such, strategies to attenuate muscle mass loss are of utmost importance in the elderly population.

We know that consuming protein-containing meals can stimulate MPS and thus maintain muscle mass over time; however, older adults are less sensitive to the stimulatory effects of protein on MPS (Pennings and others 2012). Whereas it has been established that about 20 g of high-quality protein maximally stimulates MPS in younger individuals (Moore and others 2009; Witard and others 2014), in older adults the MPS response to a given dose of protein is blunted (Moore and others 2014) and, as compared with 20 g protein, is stimulated to a greater extent by 35 and 40 g of protein at rest (Pennings and others 2012) and following exercise (Yang and others 2012a). In addition, a recent study found that, whereas protein at 0.24 g/kg BW maximally stimulated MPS in younger individuals, 0.40 g/kg BW weight was needed to maximally stimulate MPS in older adults (Moore and others 2014). As such, it has been suggested that the protein needs of older adults are greater than those of younger individuals (0.8 g/kg BW/day) and protein intakes of 1.0 to 1.5 g protein/kg BW/day are recommended for this population (Wolfe and others 2008; Bauer and others 2013). However, while data from the U.S. National Health and Nutrition Examination Survey (NHANES) show that adults are meeting, and even exceeding, the recommended dietary allowance (RDA) for protein by consuming about 1.3 g protein/kg BW/day (Fulgoni 2008), older adults are not consuming adequate amounts of protein, with one-third not meeting the RDA for protein and up to 10% of older women not even meeting the Estimated Average Requirement (EAR, 0.66 g/kg BW/day) (Houston and others 2008; Volpi and others 2013).

Compounding the problem of a blunted response to protein intakes in older adults is that most older adults consume protein in a skewed manner throughout the day, with the bulk of the protein being eaten at the evening meal (Berner and others 2013). Imbalanced protein intake is a concern given that older adults require a greater amount of protein at each meal to raise MPS levels above basal levels (Pennings and others 2012; Yang and others 2012a). With a low intake of protein at breakfast (about 12 to 15 g) and a moderate intake at lunch (about 18g), older adults are not optimally increasing MPS throughout the day, which is not ideal for the maintenance of muscle mass with aging. Recent recommendations state that older adults should consume 25 to 30 g of high-quality protein at each meal in order to ensure that MPS is maximally stimulated throughout the day (Paddon-Jones and Rasmussen 2009; Bauer and others 2013). Given these logistical issues pertaining to protein consumption, paired with a lower overall food intake, older adults are predisposed to energy-protein "undernutrition" (Morley 1997). A practical consideration would be for older adults to consume a higher-protein diet and/or to enhance their diet with a high-quality protein supplement to help offset muscle mass losses and to optimize health (Bauer and others 2013; Deutz and others 2014).

Studies have shown that higher protein intakes are protective against weight (Stookey and others 2005; Gray-Donald and others 2014) and lean mass loss (Houston and others 2008) and are positively associated with muscle mass (Stookey and others 2005; Geirsdottir and others 2013) in older adults. Similarly, a recent meta-analysis (Cermak and others 2012) found that consuming protein, either via supplement or incorporation into the habitual diet, on days when resistance exercise was performed, resulted in greater increases in muscle mass and strength as compared with placebo in older adults. In addition, 24 wk of twice daily protein supplementation (15 g each at breakfast and lunch) has been shown to improve strength and physical performance in frail elderly individuals (Tieland and others 2012b). Also, when paired with resistance training, this supplementation regime increased muscle mass in frail elderly individuals, whereas no increase in muscle mass was found in the placebo group (Tieland and others 2012a). Of note, through the use of a supplement consumed immediately after breakfast and lunch in the 2 preceding studies, the protein content of each meal was at least 25 g, which is the minimum recommended amount of protein older adults should consume at each meal to promote positive protein balance (Bauer and others 2013). Thus, a higher-protein diet is beneficial for the maintenance of lean body mass in older adults and should be recommended for this population.

In addition to consuming a higher protein diet, the quality of protein being consumed requires consideration. We (Burd and others 2012; Yang and others 2012b) and others (Pennings and others 2011) have shown that whey protein is superior to other types of protein (casein and soy) in stimulating MPS. Specifically, whey protein feeding resulted in greater MPS and less protein oxidation as compared with soy protein feeding in both the rested and post–resistance exercise state (Yang and others 2012b) in older men. Of interest, while 20 g of whey protein increased MPS rates above basal in both the rested and exercised legs with a further increase in MPS in the exercised leg with 40 g of whey protein, 20 g of soy protein did not increase MPS rates above basal in either leg and with 40 g of soy protein only increased MPS rates above basal in the exercised leg (Yang and others 2012b). Similarly, 20 g of whey protein also resulted in a greater rise in EAAs and leucine and a concomitant greater MPS response than 20 g of casein protein in both the fed-only (Pennings and others 2011; Burd and others 2012) and exercised (Burd and others 2012) state in older men. Taken together, with consideration to the fact that older adults are not consuming adequate amounts of protein, the findings of these studies suggest that the addition of whey protein supplements would be advantageous for older adults to achieve optimal stimulation of MPS throughout the day and thus decrease the severity of muscle mass loss that accompanies aging.

Higher Protein Diets to Support "High-Quality" Weight Loss

Typical energy-restricted diets, while resulting in a loss in BW also result in a loss of lean body mass (20% to 25% of total weight loss) (Krieger and others 2006). As lean body mass is a major determinant of basal metabolic rate, its loss results in a concomitant decrease in resting energy expenditure and over time can make it more difficult to lose weight and/or result in weight regain (Westerterp-Plantenga and others 2009). As such, diets that can maximize lean mass retention during weight loss are critical to weight loss success. A recent meta-analysis showed that higher protein consumption (>1.25 g/kg/d) during caloric restriction resulted in greater losses of BW and fat mass and completely attenuated decreases in lean body mass and resting energy expenditure, as compared with standard protein (0.72 g/kg/d) diets. This "high quality" weight loss, which we define as the loss of weight with the greatest amount of fat-mass loss to lean mass retention, is important in the maintenance of resting metabolic rate and prevention of weight regain. Importantly, while the percentage of energy intake from protein is higher with higher-protein, calorically restricted diets, the absolute amount of protein being consumed (about 1.2 g/kg/d) is similar to what is consumed by the general population during periods of energy balance (Fulgoni 2008).

Protein quality also plays an important role in body composition changes during energy restriction. Several prospective studies have found an inverse relationship between dairy consumption and weight gain and abdominal obesity (Pereira and others 2002; Newby and others 2003; Lutsey and others 2008). In addition, 2 recent meta-analyses of randomized controlled trials found that increased dairy consumption resulted in greater fat mass loss and lean mass retention during short-term energy restriction (Abargouei and others 2012; Chen and others 2012). In addition, waist circumference (a marker of visceral adipose tissue and metabolic health risk) was decreased to a greater extent during energy restriction with higher dairy consumption (Abargouei and others 2012). Our lab has shown that when a higher-dairy (6 to 7 servings of dairy/d), higher-protein (30% of energy intake) diet is consumed during energy restriction and exercise training (aerobic 5×/wk and resistance training 2×/wk), fat mass is lost and lean body mass can actually be increased in overweight/obese, premenopausal women (Josse and others 2011).

Whey protein, as a dairy-derived protein, is at least partially responsible for the favorable body composition changes induced by higher dairy consumption during energy deficit (Miller and others 2014). Specifically, it has been shown that when whey is supplemented into an energy restricted diet there was a greater loss in fat mass and a lesser loss in lean mass (Frestedt and others 2008). Similarly, in elderly women whey protein consumed as a replacement for other calories in a calorically restricted diet resulted in greater weight loss and a sparing of lean mass relative to BW (Mojtahedi and others 2011). In addition, as compared with a conventional meal replacement, a whey protein and EAA meal replacement resulted in greater fat mass loss in elderly individuals (Coker and others 2012). Whey protein not only plays a role in promoting weight loss during caloric restriction, but has also been shown to be more effective at maintaining weight and fat mass losses than a carbohydrate control during a period of ad libitum feeding postcaloric restriction in overweight/obese men and women (Claessens and others 2009). Lastly, while subjects were not provided with dietary advice and consumed ad libitum diets, daily supplementation with whey protein (56 g/d) was found to be superior than carbohydrate, whereas soy supplementation was not, at reducing BW and fat mass in free-living overweight/obese adults (Baer and others 2011). Thus, evidence does support a role for whey protein in promotion of "high-quality" weight loss during caloric restriction and support weight maintenance following weight loss.

Higher-protein diets also promote weight loss through increased satiety, resulting in lower ad libitum food intake (Skov and others 1999). Dairy and whey protein have both been shown to promote satiety after consumption (Pal and Ellis 2010; Lorenzen and others 2012; Jones and others 2013). Specifically, whey protein has been found to decrease rating of hunger prior to a subsequent meal (4 h after whey consumption) and ad libitum caloric consumption at a subsequent meal as compared with turkey, egg, or tuna consumption (Pal and Ellis 2010). However, another acute appetite study found that skim milk decreased energy intake at a subsequent meal to a greater extent than whey or casein proteins (Lorenzen and others 2012). The impact of dairy on appetite suppression over a longer period has also been studied in a 12-wk trial where subjects either consumed a high-dairy, high-calcium (1400 mg/d) or low-dairy, low-calcium (700 mg/d) diet during moderate caloric restriction (Jones and others 2013). The findings from this study indicated that the impact of dairy on appetite is sustainable as individuals in the dairy group were more satisfied during the caloric restriction than those in the low-dairy group (Jones and others 2013). As such, it appears that dairy and whey protein consumption can also help promote weight loss through an emerging role in appetite suppression.

Conclusion

Higher-protein diets (that is, >20% but less than 35% of total energy intake) are, in our view, integral to supporting lean body mass in young and older adults. Recent meta-analyses have shown that higher protein consumption enhances lean body mass gains during resistance exercise in both young and older individuals and promotes "high-quality" weight loss during caloric restriction. In addition, leading authorities have made recommendations for higher protein intakes for older adults to combat age-related losses of muscle mass and strength. Whey protein is the optimal protein source to support MPS at rest and following resistance exercise as well as to induce muscle hypertrophy and strength gains with resistance training. The greater effect of whey protein in supporting muscle anabolism is a function of its AA content (high EAAs, BCAAs and particularly leucine), rapid digestibility, and high bioavailability within the plasma and muscle tissue upon consumption to induce MPS. Thus, the inclusion of whey protein is an important component to optimizing body composition.

Author Contributions

M. Devries and S. Phillips drafted and reviewed the manuscript. Both authors agreed to the final content.

References

Abargouei A, Janghorbani M, Salehi-Marzijarani M, Esmailzadeh A. 2012. Effect of dairy consumption on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Int J Obes 36:1485–93.
Andersen LL, Tufekovic G, Zebris M, Crameri R, Verlaan G, Kjaer M, Suetta C, Magnusson P, Aagaard P. 2005. The effect of resistance training combined with timed ingestion of protein on muscle fiber size and muscle strength. Metabolism 54:151–6.
Anthony J, Yoshizawa F, Anthony T, Vary T, Jefferson L, Kimball S. 2000. Leucine stimulates translation initiation in skeletal muscle of postabsorptive rats via a rapamycin-sensitive pathway. J Nutr 130:2413–9.
Anthony J, Anthony T, Kimball S, Jefferson L. 2001. Signalling pathways involved in translational control of protein synthesis in skeletal muscle by leucine. J Nutr 131:856S–60S.
Areta J, Burke L, Camera D, West D, Crawshay S, Moore DR, Stellingwerff T, Phillips S, Hawley J. 2014. Reduced resting skeletal muscle protein synthesis is rescued by resistance exercise and protein ingestion following short-term energy deficit. Am J Physiol Endocrinol Metab 306:E989–E97.
Baer D, Stote K, Paul D, Harris G, Rumpler W, Clevidence B. 2011. Whey protein but not soy protein supplementation alters body weight and composition in free-living overweight and obese adults. J Nutr 141(8):1489–94.
Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft A, Morley J, Phillips S, Sieber C, Stehle P, Teta D, Visvanathan R, Volpi E, Boirie Y. 2013. Evidence-based recommendation for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc 14(8):542–59.
Berner L, Becker G, Wise M, Doi J. 2013. Characterization of dietary protein among older adults in the United States: amount, animal sources, and meal patters. J Acad Nutr Diet 113:809–15.
Biolo G, Tipton K, Klein S, Wolfe RR. 1997. An abundant supply of amino acids enhances the metabolic effect of exercise on muscle protein. Am J Physiol 273(1):E122–E9.
Bird S, Tarpenning K, Marino F. 2006. Independent and combined effets of liquid carbohydrate/essential amino acid ingestion on hormonal and muscular adaptations following resistance training in untrained men. Eur J Appl Physiol 97(2):225–38.
Boirie Y, Dangin M, Gachon P, Vasson M, Maubois J, Beaufrere B. 1997. Slow and fast dietary proteins differently modulate postprandial protein accretion. Proc Nath Acad Sci USA 94:14930–5.

Special Supplement (by invite only)

Bos C, Metges CG, C, Petzke K, Pueyo M, Morens C, Everwand J, Benamouzig R. 2003. Postprandial kinetics of dietary amino acids are the main determinant of their metabolism after soy or milk protein ingestion in humans. J Nutr 133:1308–15.

Burd N, Yang Y, Moore DR, Tang JE, Tarnopolsky MA, Phillips S. 2012. Greater stimulation of myofibrillar protein synthesis with ingestion of whey protein isolate v. micellar casein at rest and after resistance exercise in elderly men. Br J Nutr 108:958–62.

Candow DG, Burke NC, Smith-Palmer T, Burke DG. 2006. Effect of whey and soy protein supplementation combined with resistance training in young adults. Int J Sport Nutr Exerc Metab 16(3):233–44.

Cermak N, Res P, de Groot L, Saris H, van Loon L. 2012. Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a meta-analysis. Am J Clin Nutr 96:1454–64.

Chen M, Pan A, Malik V, Hu F. 2012. Effects of dairy intake on body weight and fat: a meta-analysis of randomized controlled trials. Am J Clin Nutr 96(4):735–47.

Churchward-Venne T, Breen L, Di Donato D, Hector A, Mitchell C, Moore DR, Stellingwerff T, Breuille D, Offord E, Baker S, Phillips S. 2014. Leucine supplementation of a low-protein mixed macronutrient beverage enhances myofibrillar protein synthesis in young men: a double-blind, randomized trial. Am J Clin Nutr 99(2):276–86.

Claessens M, van Baak M, Monsheimer S, Saris W. 2009. The effect of a low-fat, high-protein or high-carbohydrate ad libitum diet on weight loss maintenance and metabolic risk factors. Int J Obes 33:296–304.

Coburn JW, Housh DJ, Housh TJ, Malek MH, Beck TW, Cramer JT, Johnson GO, Donlin PE. 2006. Effects of leucine and whey protein supplementation during eight weeks of unilateral resistance training. J Strength Cond Res 20(2):284–91.

Coker R, Miller S, Schutzler S, Deutz N, Wolfe RR. 2012. Whey protein and essential amino acids promote the reduction of adipose tissue and increased muscle protein synthesis during caloric restriction-induced weight loss in elderly, obese individuals. Nutr J 11:105.

Cribb P, Williams A, Hayes A, Carey M. 2006. The effect of whey isolate on strength, body composition and plasma glutamine. Int J Sport Nutr Exerc Metab 16:494–509.

Crozier S, Kimball S, Emmert S, Anthony J, Jefferson L. 2005. Oral leucine administration stimulates protein synthesis in rat skeletal muscle. J Nutr 135:376–82.

Cuthbertson D, Smith K, Babraj J, Leese G, Waddell T, Atherton P, Wackerhage H, Taylor P, Rennie M. 2005. Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. FASEB J 19(3):422–4.

da Silva Alexandre T, de Oliveira Duarte Y, Ferreira Santos J, Wong R, Lebrao M. 2014. Sarcopenia according to the european working group on sarcopenia in older people (EWG-SOP) versus Dynapenia as a risk factor for disability in the elderly. J Nutr Health Aging 18(5):547–53.

DeFronzo R, Bonadonna R, Ferrannini E. 1992. Pathogenesis of NIDDM. A balanced overview. Diabetes Care 15(3):318–68.

DeNysschen C, Burton H, Horvath P, Leddy J, Browne R. 2009. Resistance training with soy vs whey protein supplements in hyperlipidemic males. J Int Soc Sports Nutr 6:8.

Deutz N, Bauer J, Barazzoni R, Biolo G, Boirie Y, Bosy-Westphal A, Caderholm T, Cruz-Jentoft A, Krznaric Z, Nair K, Singer P, Teta D, Tipton K, Calder P. 2014. Protein intake and exercise for optimal muscle function with aging: recommendations for the ESPEN Expert Group. Clin Nutr doi: 10.1016/j.clnu.2014.04.007.

Dreyer HC, Drummond MJ, Pennings B, Fujita S, Glynn EL, Chinkes DL, Volpi E, Rasmussen BB. 2008. Leucine-enriched essential amino acids and carbohydrate ingestion following resistance exercise enhances mTOR signaling and protein synthesis in human muscle. Am J Physiol Endocrinol Metab 294:E392–E400.

Escobar J, Frank J, Suryawan A, Nguyen H, Kimball S, Jefferson L, Davis T. 2006. Regulation of cardiac and skeletal muscle protein synthesis by individual branched-chain amino acids in neonatal pigs. Am J Physiol Endocrinol Metab 290:E612–E21.

Esmarck B, Andersen J, Olsen S, Richter E, Mizuno M, Kjaer M. 2001. Timing of postexercise protein intake is important for muscle hypertrophy with resistance training in elderly humans. J Physiol 535(1):301–11.

FAO/WHO Expert Consultation. 1991. Protein quality evaluation report of the Joint FAO/WHO Expert Consultation held in Bethseda, Md., USA, in 1989. FAO Food and Nutrition Paper 51, Rome.

Fouillet H, Mariotti F, Gaudichon C, Bos C, Tome D. 2002. Peripheral and splanchnic metabolism of dietary nitrogen are differently affected by the protein source in humans as assessed by compartmental modeling. J Nutr 132(1):125–33.

Fouillet H, Juillet B, Gaudichon C, Mariotti F, Tome D, Bos C. 2009. Absorption kinetics are a key factor regulating postprandial protein metabolism in response to qualitative and quantitative variations in protein intake. Am J Physiol Regul Integr Comp Physiol 297(6):R1691–705.

Frestedt J, Zenk J, Kuskowski M, Ward L, Bastian E. 2008. A whey-protein supplement increases fat loss and spares lean muscle in obese subjects: a randomized human clinical study. Nutr Metab 5:8.

Fulgoni V. 2008. Current protein intake in America: analysis of the Nathional Health and Nutrition Examination Survery, 2003–2004. Am J Clin Nutr 87:1554S–7S.

Geirsdottir O, Arnarson A, Ramel A, Jonsson P, Thorsdottir I. 2013. Dietary protein intake is associated with lean body mass in community-dwelling older adults. Nutr Res 33(8):608–12.

Gray-Donald K, St-Arnauld-McKenzie D, Gaudreau P, Morais J, Shatenstein B, Payette H. 2014. Protein intake protects against weight loss in healthy community-dwelling older adults. J Nutr 144(3):321–6.

Hartman J, Tang JE, Wilkinson S, Tarnopolsky M, Lawrence R, Fullerton A, Phillips S. 2007. Consumption of fat-free fluid milk after resistance exercise promotes greater lean mass accretion than does consumption of soy or carbohydrate in young, novice, male weightlifters. Am J Clin Nutr 86(2):373–81.

Hoffman JR, Ratamess NA, Tranchina CP, Rashti SL, Kang J, Faigenbaum AD. 2009. Effect of protein-supplement timing on strength, power, and body-compsition changes in resistance-trained men. Int J Sport Nutr Exerc Metab 19(2):172–85.

Houston D, Nicklas B, Ding J, Harris T, Tylavsky F, Newman A, Lee J, Sahyoun N, Visser M, Kritchevsky S, Health ABC Study. 2008. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr 87(1):150–5.

Hulmi J, Koyanen V, Selanne H, Kraemer W, Hakkinen K, Mero A. 2009. Acute and long-term effects of resistance exercise with or without protein ingestion on muscle hypertrophy and gene expression. Amino Acids 37:297–308.

Jones K, Eller L, Parnell J, Doyle-Baker P, Edwards A, Reimer R. 2013. Effect of a dairy- and calcium-rich diet on weight loss and appetite during energy restriction in overweight and obese adults: a randomized trial. Eur J Clin Nutr 67(4):371–6.

Josse AR, Atkinson SA, Tarnopolsky MA, Phillips SM. 2011. Increased consumption of dairy foods and protein during diet- and exercise-induced weight loss promotes fat mass loss and lean mass gain in overweight and obese premenopausal women. J Nutr 141(9):1626–34.

Joy J, Lowery R, Wilson J, Purpura M, De Souza E, Wilson S, Kalman D, Dudeck J, Jager R. 2013. The effects of 8 weeks of whey or rice protein supplementation on body composition and exercise performance. Nutr J 12:86.

Jurca R, Lamonte M, Barlow C, Kampert J, Church T, Blair S. 2005. Association of muscular strength with incidence of metabolic syndrome in men. Med Sci Sports Exer 37(11):1849–55.

Karagounis L, Hawley J. 2010. Skeletal muscle: increasing the size of the locomotor cell. Int J Biochem Cell Biol 42(9):1376–9.

Katsanos C, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR. 2006. A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. Am J Physiol Endocrinol Metab 291:E381–E7.

Koopman R, Wagenmakers AJ, Manders RJ, Zorenc AH, Senden JM, Gorselink M, Keizer HA, van Loon LJ. 2005. Combined ingestion of protein and free leucine with carbohydrate increases postexercise muscle protein synthesis in vivo in male subjects. Am J Physiol Endocrinol Metab 288:E645–E53.

Krieger J, Sitren H, Daniels M, Langkamp-Henken B. 2006. Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: a meta-regression. Am J Clin Nutr 83:260–74.

Landi F, Liperoti R, Russo A, Giovannini S, Tosato M, Capoluongo E, Bernabei R, Onder G. 2012. Sarcopenia as a risk factor for falls in elderly individuals: results from the il SIRENTE study. Clin Nutr 31(5):652–8.

Lorenzen J, Frederiksen R, Hoppe C, Hvid R, Astrup A. 2012. The effect of milk proteins on appetite regulation and diet-induced thermogenesis. Eur J Clin Nutr 66:622–7.

Luiking Y, Deutz N, Jakel M, Soeters P. 2005. Casein and soy protein meals differentially affect whole-body and splanchnic protein metabolism in healthy humans. J Nutr 135:1080–7.

Lutsey P, Steffen L, Stevens J. 2008. Dietary intake and the development of the metabolic syndrome: the Atherosclerosis Risk in Communities study. Circulation 117:754–61.

Miller P, Alexander D, Perez V. 2014. Effects of whey protein and resistance exercise on body composition: a meta-analysis of randomized controlled trials. J Am Coll Nutr 33(2):163–75.

Mojtahedi M, Thorpe M, Karampinos D, Johnson C, Layman D, Georgiadis J, Evans E. 2011. The effects of a higher protein intake during energy restriction and changes in body composition and physical function in older women. J Gerontol A Biol Sci Med Sci 66A(11):1218–25.

Moore D, Robinson M, Fry J, Tang J, Glover E, Wilkinson S, Prior T, Tarnopolsky M, Phillips S. 2009. Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. Am J Clin Nutr 89(1):161–8.

Moore D, Churchward-Venne T, Witard O, Breen L, Burd N, Tipton K, Phillips S. 2014. Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. J Gerontol A Biol Sci Med Sci doi:10.1093/gerona/glu103.

Morley J. 1997. Anorexia of aging: physiologic and pathologic. Am J Clin Nutr 66(4):760–73.

Newby P, Muller D, Hallfrisch J, Qiao N, Andres R, Tucker K. 2003. Dietary patterns and changes in body mass index and waist circumference in adults. Am J Clin Nutr 77(6):1417–25.

Paddon-Jones D, Rasmussen B. 2009. Dietary protein recommendations and the prevention of sarcopenia. Curr Opin Clin Nutr Metab Care 12:86–90.

Pal S, Ellis V. 2010. The acute effects of four protein meals on insulin, glucose, appetite and energy intake in lean men. Br J Nutr 104:1241–8.

Pasiakos SM, Vislocky LM, Carbone JW, Altieri N, Konopelski K, Freake HC, Anderson JM, Ferrando AA, Wolfe RR, Rodriguez NR. 2010. Acute energy deprivation affects skeletal muscle protein synthesis and associated intracellular signaling proteins in physically active adults. J Nutr 140:745–51.

Pennings B, Boirie Y, Senden J, Gijsen A, Kuipers H, van Loon L. 2011. Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men. Am J Clin Nutr 93(5):997–1005.

Pennings B, Groen B, de Lange A, Gijsen A, Zorenc A, Senden J, van Loon L. 2012. Amino acid absorption and subsequent muscle protein accretion following graded intakes of whey protein in elderly men. Am J Physiol Endocrinol Metab 302(8):E992–E9.

Pereira M, Jacobs DJ, Van Horn L, Slattery M, Kartashov A, Ludwig D. 2002. Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA study. JAMA 287(16):2081–9.

Phillips S. 2009. Physiologic and molecular bases of muscle hypertrophy and atrophy: impact of resistance exercise on human skeletal muscle (protein and exercise dose effects). Appl Physiol Nutr Metab 34:403–10.

Phillips S. 2014. A brief review of critical processes in exercise-induced muscular hypertrophy. Sports Med 44(1):71–7.

Phillips S, Tipton K, Aarsland A, Wolf S, Wolfe RR. 1997. Mixed muscle protein synthesis and breakdwon after resistance exercise in humans. Am J Physiol 273(1):E99–E107.

Ruiz J, Sui X, Lobelo F, Morrow JJ, Jackson A, Sjostrom M, Blair S. 2008. Association between muscular strength and mortality in men: prospective cohort study. BMJ 337:a439.

Schoenfeld B, Aragon A, Krieger J. 2013. The effect of protein timing on muscle strength and hypertrophy: a meta-analysis. J Int Soc Sports Nutr 10:53.

Scott D, Hayes A, Sanders K, Aitken D, Ebeling P, Jones G. 2014. Operational definitions of sarcopenia and their associations with 5-year changes in falls risk in community-dwelling middle-aged and older adults. Osteoporosis Int 25(1):187–93.

Skov A, Toubro S, Ronn B, Holm L, Astrup A. 1999. Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. Int J Obes Relat Metab Disord 23(5):528–36.

Stark M, Lukaszuk J, Prawitz A, Salacinski A. 2012. Protein timing and its effects on muscular hypertophy and strength in individuals engaged in weight-training. J Int Soc Sports Nutr 9:54.

Stookey J, Adair L, Popkin B. 2005. Do protein and energy intakes explain long-term changes in body composition? J Nutr Health Aging 9(1):5–17.

Tang JE, Phillips S. 2009. Maximizing muscle protein anabolism: the role of protein quality. Curr Opin Clin Nutr Metab Care 12(1):66–71.

Tang JE, Moore DR, Kujbida G, Tarnopolsky M, Phillips S. 2009. Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. J Appl Physiol 107(3):987–92.

Tieland M, Dirks M, van der Zwaluw N, Verdijk L, van de Rest O, de Groot L, van Loon L. 2012a. Protein supplementation increases muscle mass gain during prolonged resistance-type exercise training in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc 13(8):713–9.

Tieland M, van de Rest O, Dirks M, van der Zwaluw N, Mensink M, van Loon L, de Groot L. 2012b. Protein supplementation improves physical performance in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc 13:720–6.

Tipton K, Elliot T, Cree M, Wolf S, Sanford A, Wolfe RR. 2004. Ingestion of casein and whey proteins result in muscle anabolism after resistance exercise. Med Sci Sports Exer 36(12):2073–81.

Tipton K, Elliot T, Cree M, Aarsland A, Sanford A, Wolfe RR. 2007. Stimulation of net muscle protein synthesis by whey protein ingestion before and after exercise. Am J Physiol Endocrinol Metab 292(1):E71–E6.

United States Department of Agriculture. The USDA National Nutrient Database for Standard Reference. Nutrient Data Laboratory: Beltsville Human Nutrition Research Centre. http://ndb.nal.usda.gov/. Lastmodified Dec 7, 2011.

Velazquez Alva Mdel C, Irigoyen Camacho M, Delgadillo Velazquez J, Lazarevich I. 2013. The relationship between sarcopenia, undernutrition, physical mobility and basic activities of daily living in a group of elderly women of Mexico City. Nutr Hosp 28(2):514–21.

Verdijk L, Jonkers R, Gleeson B, Beelen M, Meijer K, Savelberg H, Wodzig W, Dendale P, van Loon L. 2009. Protein supplementation before and after exercise does not further augment skeletal muscle hypertrophy after resistance training in elderly men. Am J Clin Nutr 89(2):608–16.

Volek J. 2004. Influence of nutrition on responses to resistance training. Med Sci Sports Exer 36:689–96.

Volek J, Volk B, Gomez A, Kunces L, Jupchak B, Freidenreich D, Aristizabal J, Saenz C, Dunn-Lewis C, Ballard K, Quann E, Kawiecki D, Flanagan S, Comstock B, Fragala M, Earp J, Fernandez M, Bruno R, Ptolemy A, Kellogg M, Maresh C, Kraemer W. 2013. Whey protein supplementation during resistance training augments lean body mass. J Am Coll Nutr 32(2):122–35.

Volpi E, Mittendorpher B, Rasmussen B, Wolfe RR. 2000. The response of muscle protein anabolism to combined hyperaminoacidemia and glucose-induced hyperinsulinemia is impaired in the elderly. J Clin Endocrinol Metab 85:4481–90.

Volpi E, Campbell WW, Dwyer JT, Johnson MA, Jensen GL, Morley JE, Wolfe RR. 2013. Is the optimal level of protein intake for older adults greater than the recommended dietary allowance? J Gerontol A Biol Sci Med Sci 68(6):677–81.

West D, Burd N, Coffey V, Baker S, Burke L, Hawley J, Moore DR, Stellingwerff T, Phillips S. 2011. Rapid aminoacidemia enhances myofibrillar protein synthesis and anabolic intramuscular signaling repsonses after resistance exercise. Am J Clin Nutr 94(3):795–803.

Westerterp-Plantenga M, Nieuwenhuizen A, Tome D, Soenen S, Westerterp K. 2009. Dietary protein, weight loss, and weight maintenance. Annu Rev Nut 29:21–41.

Wilkinson S, Tarnopolsky M, MacDonald M, Macdonald J, Armstrong D, Phillips S. 2007. Consumption of fluid skim milk promotes greater muscle protein accretion after resistance exercise than does consumption of an isonitrogenous and isoenergetic soy-protein beverage. Am J Clin Nutr 85(4):1031–40.

Witard O, Jackman S, Breen L, Smith K, Selby A, Tipton K. 2014. Myofibrillar muscle protein synthesis rates subsequent to a meal in response to increasing doses of whey protein at rest and after resistance exercise. Am J Clin Nutr 99(1):86–95.

Wolfe RR. 2006. The underappreciated role of muscle in health and disease. Am J Clin Nutr 84:475–82.

Wolfe RR, Miller S, Miller K. 2008. Optimal protein intake in the elderly. Clin Nutr 27(5):675–84.

Wycherley T, Noakes M, Clifton P, Cleanthous X, Keogh J, Brinkworth G. 2010. Timing of protein ingestion relative to resistance exercise training does not influence body composition, energy expenditure, glycaemic control or cardiometabolic risk factors in a hypocaloric, high protein diet in patients with type 2 diabetes. Diab Obes Metab 12(12):1097–105.

Wycherley T, Moran L, Clifton P, Noakes M, Brinkworth G. 2012. Effects of energy-restricted high-protein, low-fat compared with standard-protein, low fat diets: a meta-analysis of randomized controlled trials. Am J Clin Nutr 96(6):1281–98.

Yang Y, Breen L, Burd N, Hector A, Churchward-Venne TJ, AR, Tarnopolsky M, Phillips S. 2012a. Resistance exercise enhances myofibrillar protein synthesis with graded intakes of whey protein in older men. Br J Nutr 108(10):1780–8.

Yang Y, Churchward-Venne T, Burd N, Breen L, Tarnopolsky MA, Phillips S. 2012b. Myofibrillar protein synthesis following ingestion of soy protein isolate at rest and after resistance exercise in elderly men. Nutr Metab (Lond) 9:57.