Aging is associated with many changes in body composition, including reduction of lean body mass with a concomitant increase in fat mass. These changes often have a negative impact on overall health and functional capacity.

Sarcopenia is the degenerative loss of skeletal muscle and strength, beginning as early as age 30, and accelerating with advancing age. Advancing sarcopenia is associated with increased risk of fall and fractures, decreased ability to complete activities of daily living, and increase in fatigue, which all lead to dependency and disability.

A lifestyle behavior that positively affects muscle mass is consumption of dietary protein. Longitudinal studies have shown that older people who consume higher amounts of protein lose less lean muscle mass over 3 years than those who eat lower amounts (eg, 91 g/day vs 57 g/day). Protein quality, quantity, and timing of consumption throughout the day and in conjunction with physical activity are all important to maintenance of muscle mass. Protein sources of high biologic value, namely those from animal sources, will provide the highest concentration of branched-chain amino acids such as leucine, which stimulate muscle protein synthesis.

Milk proteins, whey and casein, are shown to stimulate muscle protein synthesis. Both are high-quality proteins and should be consumed daily. However, they produce a different response in young people than they do in older people. Whey, for instance, is digested faster than casein and produces a relatively better response on protein balance in older people. Casein has the opposite effect and has a better response in younger people.
The goal of protein consumption and lean body mass gains is to optimize muscle protein synthesis. The quantity of essential amino acids (EAAs) is critical to elicit muscle protein synthesis. Elderly people may require 20–30 g of high-quality protein containing at least 8 g of EAAs, including leucine, three or four times a day. Another strategy to maximize muscle protein synthesis is consumption of protein-rich meals more frequently, every 2 or 3 hours.

Leucine is the primary amino acid regulator that “turns on” protein synthesis in the cells, signaling that quality protein is available for protein synthesis. Research shows that adding leucine to a meal that combines carbohydrate and protein is not necessary to get a response in protein synthesis in younger people, but it is necessary to get the same response in older people. These results suggest that the protein-synthesis response is blunted in older people when a meal combines carbohydrate with protein. Reducing simple carbohydrates may be an advantageous strategy to maximize protein synthesis, because this also is shown to reduce loss of lean tissue for people with a negative caloric intake.

A minor metabolite of L-leucine, beta-hydroxy-beta-methylbutyrate (HMB), is a precursor of cholesterol synthesis in skeletal muscle and plays a role in the control of protein homeostasis (Fig 1).
HMB is shown to decrease protein degradation by downregulation of the ubiquitin-proteasome system (Fig 2).\textsuperscript{14} It also is shown to stimulate protein synthesis by activation of mammalian target of rapamycin (mTOR), a serine/threonine protein kinase.\textsuperscript{15,16}

Fig 2. Role of HMB in protein synthesis and degradation. NFκB=nuclear factor κB

Oral administration of HMB is strongly associated with increased strength and lean body mass (LBM) and with decreased fat mass in young- to middle-aged people when combined with resistance exercise. HMB has also been shown to have clinical benefit in a number of muscle wasting/cachectic conditions and in limb immobilization.\textsuperscript{14,17,18} These mechanisms appear to be relevant to older people, and clinical studies have demonstrated decreases in body fat percentage, gains in lower- and upper-body strength, increases in limb circumference, leg and handgrip strength, and increases in “get-up-and-go” performance with HMB.\textsuperscript{13,19,20} The get-up-and-go functionality assessment involves measuring the time it takes a person to rise from a chair, walk a specified distance, and then return to the chair.
Fig 3 shows the improvements in functionality that resulted when 50 elderly women were supplemented with 2 g HMB, along with arginine and lysine, daily for 12 weeks.\footnote{19}

![Fig 3. Changes in functionality after 12 weeks of supplementation with HMB+ (HMB, arginine, and lysine) compared to controls.\textsuperscript{19} sec=seconds](image)

After 12 weeks of supplementation, the “get-up-and-go” functionality test results improved by 17% in the experimental group (2.3 +/- 0.5 seconds), but did not change in the placebo group ($P=0.002$). Improved functionality also was reflected in increased limb circumference, leg strength, and handgrip strength (each $P<0.05$).

The current recommended dosage for HMB is 3 g/day.\footnote{13} This recommendation is based on the finding that increasing HMB from 1.5 g to 3 g increases strength and LBM, while doses greater than 3 g/day do not have an additional effect.\footnote{13}

Exercise also is known to increase muscle mass. Muscle mass gains can be maximized by combining the consumption of protein, amino acids, or HMB in close proximity to a session of resistance exercise. An increase in muscle protein synthesis can last up to 36 to 48 hours after a bout of intense exercise. Providing amino acids immediately before or after exercise can increase muscle protein synthesis approximately 2.5 times greater than the effect from exercise alone.\footnote{21,22}

In the elderly, consumption of protein has to occur immediately after exercise to realize the benefits.\footnote{21-23}
In summary, several lifestyle strategies are recommended to promote optimal muscle protein synthesis, including consumption of the following:

- Adequate amounts of high-quality protein, essential amino acids/branched-chain amino acids/leucine, and supplemental HMB
- Protein-rich meals and snacks every 2–3 hours to maximize muscle protein balance
- Moderate amounts of carbohydrate for energy (insulin secretion) and to spare protein from being used for energy
- Foods containing a mixture of protein and carbohydrates 40–120 minutes before exercise and immediately after exercise to increase strength and hypertrophy

References

Nutrition, Muscle Mass, and Muscular Performance in Middle Age and Beyond


