

What is the Optimal Amount of Protein to Support Post-Exercise Skeletal Muscle Reconditioning in the Older Adult?

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Abstract Hyperaminoacidemia following protein ingestion enhances the anabolic effect of resistance-type exercise by increasing the stimulation of muscle protein synthesis and attenuating the exercise-mediated increase in muscle protein breakdown rates. Although factors such as the source of protein ingested and the timing of intake relative to exercise can impact post-exercise muscle protein synthesis rates, the amount of protein ingested after exercise appears to be the key nutritional factor dictating the magnitude of the muscle protein synthetic response during post-exercise recovery. In younger adults, muscle protein synthesis rates after resistance-type exercise respond in a dose-dependent manner to ingested protein and are maximally stimulated following ingestion of ~20 g of protein. In contrast to younger adults, older adults are less sensitive to smaller doses of ingested protein (less than ~20 g) after exercise, as evidenced by an attenuated increase in muscle protein synthesis rates during post-exercise recovery. However, older muscle appears to retain the capacity to display a robust stimulation of muscle protein synthesis in response to the ingestion of greater doses of protein (~40 g), and such an amount may be required for older adults to achieve a robust stimulation of muscle protein synthesis during post-exercise recovery. The aim of this article is to discuss the current state of evidence regarding

the dose-dependent relationship between dietary protein ingestion and changes in skeletal muscle protein synthesis during recovery from resistance-type exercise in older adults. We provide recommendations on the amount of protein that may be required to maximize skeletal muscle reconditioning in response to resistance-type exercise in older adults.

Key Points

Ingestion of ~20 g of protein is sufficient to maximize skeletal muscle protein synthesis rates during recovery from resistance type exercise in younger adults.

As opposed to younger adults, stimulation of muscle protein synthesis in older adults increases, even up to levels of intake of ~40 g of protein during recovery from resistance-type exercise.

Although there is currently no consensus on the amount of protein required to maximally stimulate skeletal muscle protein synthesis rates during recovery from resistance-type exercise in older adults, the 'optimal' dose of ingested protein may be double (~40 g) that required by younger adults.

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1 Introduction

Resistance-type exercise training results in profound increases in skeletal muscle mass, strength, power, and metabolic function. The marked physiologic and biochemical adaptations induced by resistance-type exercise training

can be augmented by dietary protein ingestion as skeletal muscle is nutritionally responsive to amino acid availability. Protein-derived amino acids serve to enhance the rate of protein synthesis and, to a lesser extent, suppress the rate of protein breakdown indirectly via their capacity to increase endogenous insulin release. The postprandial increase in muscle protein synthesis appears to be regulated almost exclusively by the increase in essential amino acid (EAA) availability [1]. Although factors such as the source of dietary protein ingested [2, 3], timing of protein intake relative to exercise [4], and post-prandial amino acid delivery profile [5, 6] may modulate muscle protein synthesis rates, the amount of protein (and constituent EAAs) ingested after exercise is arguably the key nutritional factor dictating the magnitude of the post-exercise muscle protein synthesis response. To date, dose-response studies in both younger [7, 8] and older [9–11] adults have been undertaken in an effort to identify the dose of protein that should be ingested after exercise to facilitate a (near) maximal stimulation of muscle protein synthesis rates during acute post-exercise recovery. Specifically, in younger adults, muscle protein synthesis rates after resistance-type exercise respond in a dose-dependent manner to ingested protein and are maximally stimulated following ingestion of only ~20 g of a high-quality ('high quality' is defined here as a Digestible Indispensable Amino Acid Score >1.0) protein [7, 8]. However, the dose of ingested protein required to elicit a maximal stimulation of muscle protein synthesis rates during recovery from resistance-type exercise in older adults has not been clearly defined [9–11]. Older adults display anabolic resistance to amino acid intake [12] and resistance-type exercise [13] which manifests as a reduced muscle protein synthetic response following exposure to these stimuli [14]. This age-related anabolic resistance can be seen in the relatively larger doses of protein (~40 g) that are necessary for older adults to achieve a robust stimulation of muscle protein synthesis during recovery from resistance-type exercise [9–11]. Thus, the dose of protein needed to robustly stimulate skeletal muscle protein synthesis is twice as high in older adults as in younger adults.

The aim of this opinion article is to discuss the current state of evidence regarding the dose-dependent relationship between the amount of protein ingested and the increase in skeletal muscle protein synthesis rate following resistance-type exercise. Specific emphasis will be placed on observed differences in the sensitivity and capacity of older adults, relative to younger adults, to increase muscle protein synthesis rates after resistance-type exercise when increasing amounts of dietary protein are ingested. Older athletes and exercisers who employ nutritional strategies that take into account optimal protein intake after acute exercise place themselves in a better position to adaptively respond to each exercise session, thereby facilitating

increases in muscle mass and strength, and improving training efficiency over time [15, 16].

2 Why Dietary Protein is Critical for Resistance Exercise to Facilitate Muscle Anabolism

In healthy, non-exercising adults, muscle mass remains relatively constant since muscle protein synthesis and breakdown are in dynamic equilibrium on a day-to-day basis. When an individual adheres to a program of resistance-type exercise training, skeletal muscle hypertrophy occurs as a result of muscle protein synthesis rates chronically exceeding muscle protein breakdown rates. When performed in the post-absorptive state, resistance-type exercise stimulates rates of both muscle protein synthesis [17] and muscle protein breakdown, but to a lesser extent than synthesis [18]. Under such conditions, there is a less negative, but still not positive, net protein balance. When protein is provided after resistance-type exercise, the ensuing hyperaminoacidemia further stimulates muscle protein synthesis as the amino acids are used for *de novo* muscle protein synthesis [19]. In addition, protein ingestion stimulates endogenous insulin release that can lower the exercise-stimulated increase in muscle protein breakdown [20]. Therefore, protein ingestion following resistance-type exercise results in a positive net-protein balance and is necessary for resistance-type exercise to serve as a net anabolic stimulus for skeletal muscle. Given that protein ingestion can further stimulate muscle protein synthesis, and is critical to induce a positive net protein balance following resistance-type exercise, a common question among athletes and exercisers is 'How much protein should I ingest after a workout/training session to maximize the adaptive response to resistance-type training?' The answer to this question is not entirely clear but appears to depend on age [7–11], bodyweight [21], energy balance [22], and possibly training status [16].

3 Ingested Protein Dose to Maximize Skeletal Muscle Reconditioning After Resistance-Type Exercise in Younger Adults

To date, two studies have investigated the dose-response relationship between protein ingestion and muscle protein synthesis rates following resistance-type exercise in younger adults [7, 8]. The studies differed in several aspects, including the source of dietary protein provided post-exercise, the active muscle mass during exercise, the choice of amino acid tracer, and the skeletal muscle protein fractions that were investigated (Table 1). However, a similar response was observed in that ingestion of ~20 g

Table 1 Summary of studies examining the dose-response relationship between protein ingestion and muscle protein synthesis (FSR) following resistance-type exercise in younger and older men

Study	Sex	Age, years (mean ± SD)	Subjects, study design	Model	Protein source	Protein amounts (g/kg BW)	Incorporation time (min)	Tracer, precursor product	Exercise FSR (%·h ⁻¹) [mean ± SEM]
Younger subjects									
Moore et al. [7]	Male	22 ± 5	n = 6 1 Group Crossover	Bilateral RE Leg press Leg curl Leg extension 4 sets	Whole egg	5 g: 0.058	180	[1- ¹³ C]Leucine	0 g: 0.056 ± 0.007
						10 g: 0.12			5 g: 0.074 ± 0.008 (+32 %)
						20 g: 0.23 40 g: 0.46			10 g: 0.088 ± 0.011 (+57 %) 20 g: 0.107 ± 0.011 (+91 %) 40 g: 0.116 ± 0.011 (+107 %)
Witard et al. [8]	Male	21 ± 2	n = 12 4 Groups Parallel	Unilateral RE Leg press Leg extension 8 sets 10 repetitions	Whey isolate	10 g: 0.12	240	[ring- ¹³ C ₆]Phenylalanine Arterialized blood Myofibrillar protein	0 g: 0.051 ± 0.004
						20 g: 0.24			10 g: 0.059 ± 0.003 (+17 %)
						40 g: 0.50			20 g: 0.070 ± 0.003 (+37 %) 40 g: 0.077 ± 0.003 (+51 %)
Older subjects									
Robinson et al. [9]	Male	59 ± 12	n = 6-7 4 Groups Parallel	Unilateral RE Leg extension 3 sets 8-10 repetitions	Beef	12 g: 0.15	240	[ring- ¹³ C ₆]Phenylalanine IC free AA Myofibrillar protein	0 g: 0.031 ± 0.004
						24 g: 0.30			12 g: 0.035 ± 0.004 (+13 %)
						36 g: 0.44			24 g: 0.042 ± 0.003 (+35 %) 36 g: 0.062 ± 0.013 (+100 %)
Yang et al. [11]	Male	71 ± 4	n = 7-10 4 Groups Parallel	Unilateral RE Leg extension 3 sets 10 repetitions	Whey isolate	10 g: 0.13	240	[ring- ¹³ C ₆]Phenylalanine IC free AA Myofibrillar protein	0 g: 0.043 ± 0.010
						20 g: 0.25			10 g: 0.049 ± 0.007 (+14 %)
						40 g: 0.49			20 g: 0.062 ± 0.010 (+44 %) 40 g: 0.082 ± 0.026 (+91 %)
Yang et al. [10]	Male	71 ± 5	n = 10 3 Groups Parallel	Unilateral RE Leg extension 3 sets 10 repetitions	Soy isolate	20 g: 0.26	240	[ring- ¹³ C ₆]Phenylalanine IC free AA Myofibrillar protein	0 g: 0.031 ± 0.007
						40 g: 0.52			20 g: 0.041 ± 0.010 (+29 %)
									40 g: 0.056 ± 0.009 (+81 %)

FSR data were obtained from the studies cited in the table [7-11]

AA amino acids, α-KIC alpha ketoisocaproate, BW bodyweight, FSR fractional synthetic rate, IC intracellular, RE resistance-type exercise, SD standard deviation, SEM standard error of the mean

dietary protein (corresponding to ~ 10 g EAA) was sufficient to elicit a near maximal stimulation of muscle protein synthesis rates during early post-exercise recovery. Doubling the amount of ingested protein to 40 g resulted in a non-significant ~ 8 % [7] and ~ 9 % [8] increase in muscle protein synthesis, and was associated with an enhanced rate of leucine oxidation [7] and urea formation [8]. These findings suggest that there is a maximal rate at which muscle protein can be synthesized when protein is ingested after exercise, and that ingestion of a dose of protein greater than ~ 20 g does little to further stimulate muscle protein synthesis rates. Deutz and Wolfe [23] recently discussed that a certain amount of protein-derived amino acids is retained in the splanchnic region (splanchnic extraction) following protein ingestion, and may be released over time and eventually incorporated into various tissues such as skeletal muscle. As such, measurement of the acute muscle protein synthesis response following protein ingestion may underestimate the total anabolic response over time [23]. Using intrinsically L-[1- 13 C]phenylalanine-labeled dietary proteins, it was reported that ~ 50 % of the protein-derived amino acids becomes available in the systemic circulation during the first 4–6 h after ingesting 20 g protein [19]. This implies that a large proportion of the ingested protein is retained in splanchnic tissues and/or used for intestinal and/or hepatic tissue protein synthesis. However, previous work from our laboratory [24] has been unable to find evidence that greater amounts of dietary protein-derived amino acids retained in the gut are released at a later stage, at least not in substantial amounts.

Studies in which absolute doses of protein are provided do not account for potentially important differences in body (and lean tissue) mass between individuals. For example, the optimal protein dose to maximize muscle protein synthesis rates after resistance-type exercise might differ between a 105 kg male weightlifter compared with a 69 kg male weightlifter. Recently, Moore and colleagues estimated that a per-meal feeding of ~ 0.25 g protein/kilogram bodyweight is sufficient to maximally stimulate muscle protein synthesis in younger adults, although these data were obtained from unexercised muscle [21]. However, using the example above, a more individually tailored protein dosing strategy might result in the 105 kg weightlifter ingesting ~ 26 g protein, whereas the 69 kg weightlifter might only need approximately ~ 17 g protein to elicit a maximal muscle protein synthetic response after exercise. In addition to differences in body mass, the amount of skeletal muscle tissue that is actively recruited during an exercise session may modulate protein requirements after resistance-type exercise as more of the ingested protein-derived amino acids will be used for de novo protein synthesis in exercised muscle [19]. Although it is somewhat intuitive that female athletes, who generally

possess less muscle mass than their male counterparts, may require a lower dose of ingested protein to maximally stimulate muscle protein synthesis, to date there are no data available on the optimal dose of ingested protein to maximize muscle protein synthesis after exercise in females. Although there is no health risk to younger healthy female athletes who might ‘overconsume’ protein by adhering to absolute protein dose recommendations generated from resistance-trained males [7, 8], a more tailored approach for younger female athletes with reduced body mass might be to adhere to per-meal feedings of ~ 0.25 g protein/kilogram bodyweight [21]. As an example, this would result in a 53 kg female weightlifter ingesting ~ 13 g protein after a training session.

Many athletes and exercisers reduce their energy intake while training in order to alter their body composition for aesthetic purposes and/or to improve performance (compete in desired weight class, improve power-to-weight ratio). However, energy intake restriction often results in the loss of lean body mass, leading to decrements in training capacity and/or performance and increased injury risk [25]. The dose of ingested protein necessary to induce a maximal stimulation of muscle protein synthesis after resistance-type exercise appears to increase during conditions of energy deficit compared with conditions of energy balance [22]. For example, Areta and co-workers demonstrated greater rates of muscle protein synthesis in response to 30 versus 15 g of whey protein when ingested after resistance-type exercise performed under conditions of mild energy deficit (energy availability of $30 \text{ kcal}\cdot\text{kg fat-free mass}^{-1}\cdot\text{day}^{-1}$). Therefore, energy deficit appears to induce a form of anabolic resistance in that ingestion of higher doses of protein are necessary to achieve a robust stimulation of muscle protein synthesis during recovery from resistance-type exercise. Whether a more severe energy deficit further reduces the capacity of skeletal muscle to mount an anabolic response to lower doses of ingested protein and/or increases the dose of ingested protein required to maximize muscle protein synthesis remains to be investigated. Younger athletes and exercisers seeking to retain muscle mass during periods of energy intake restriction may benefit from doses of dietary protein close to ~ 30 g after exercise to induce a more robust stimulation of muscle protein synthesis rates during post-exercise recovery.

4 Ingested Protein Dose to Maximize Skeletal Muscle Reconditioning After Resistance-Type Exercise in Older Adults

Current evidence suggests that the nutrient sensitivity of older adults to the muscle protein stimulatory effects of protein ingestion is attenuated compared with younger

adults (for review see Churchward-Venne et al. [26]). However, no studies to date have directly compared the dose-response relationship between protein ingestion and skeletal muscle protein synthesis rates between younger and older adults during recovery from resistance-type exercise. When comparing across studies, older adults appear to demonstrate an attenuated post-exercise muscle protein synthetic response following the ingestion of smaller doses (<20 g) of dietary protein when compared with younger adults [9–11]. To date, three studies examining the dose-response relationship between protein ingestion and post-exercise muscle protein synthesis rates have been conducted in older adults [9–11]. Collectively, these studies yielded similar findings in that ingestion of ~40 g protein during recovery from resistance-type exercise stimulated a greater muscle protein synthetic response post-exercise when compared with the ingestion of 20 g protein, regardless of whether the ingested protein source was whey [11], soy [10], or beef [9]. For example, ingesting ~36 g protein from beef resulted in a ~100 % increase in muscle protein synthesis rates compared with the ~35 % increase observed after ingesting 24 g protein from beef after resistance-type exercise (Table 1). However, as can be seen in Table 1, the exercise stimulus applied in the dose-response studies performed in younger adults [7, 8], is substantially greater than the exercise stimulus applied in the dose-response studies performed in older adults [9–11]. Kumar and colleagues [27] reported that doubling resistance-type exercise volume (from three to six sets), regardless of exercise load (40 or 75 % single repetition maximum), increased muscle protein synthesis rates during post-exercise recovery in older adults but not younger adults. Therefore, a greater resistance-type exercise stimulus (more working sets) in older adults may serve to further stimulate skeletal muscle protein synthesis rates and render them comparable to those seen in younger adults.

Current data on the absolute dose of ingested protein that appears to be required to robustly stimulate muscle protein synthesis rates after resistance-type exercise in older adults aligns with recently reported per-meal feeding estimates of ~0.40 g protein/kilogram bodyweight to maximally stimulate muscle protein synthesis rates under resting conditions in older individuals [21]. In support of this per-meal protein recommendation, recent data from Norton and colleagues [28] demonstrated that increased protein intake at breakfast (from 0.23 ± 0.1 to 0.40 ± 0.1 g protein/kilogram bodyweight) and lunch (from 0.31 ± 0.2 to 0.47 ± 0.2 g protein/kilogram bodyweight) significantly increased whole-body lean mass (~0.5 kg) over 24 weeks in older adults. Together, these

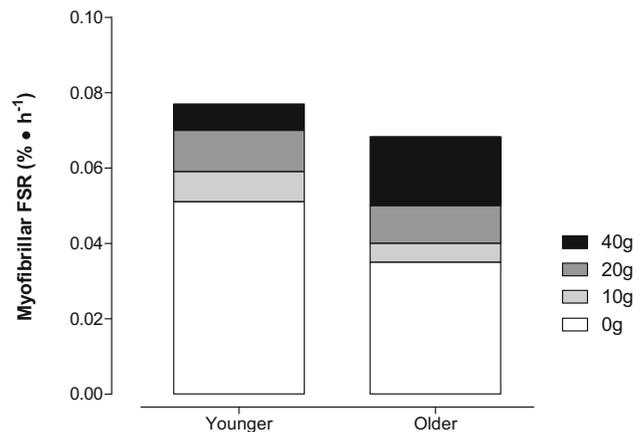


Fig. 1 Myofibrillar FSRs during recovery from resistance-type exercise in response to 0, 10, 20, and 40 g protein in younger and older adults, as derived from Witard et al. [8], Yang et al. [10, 11], Robinson et al. [9] and Table 1. Note, data from Moore et al. [7] were not included since mixed muscle protein synthesis was determined in that study. *FSR* fractional synthesis rates

findings suggest that skeletal muscle in older adults retains the capacity for robust increases in muscle protein synthesis rates (Fig. 1), but that a greater amino acid/protein stimulus is necessary [21]. It is important to highlight that a clear plateau in muscle protein synthesis rates in response to the ingestion of graded doses of protein after resistance-type exercise has not yet been identified in older adults. As such, it may be that doses of protein greater than ~40 g may further stimulate an increase in muscle protein synthesis rates in older adults following resistance-type exercise. However, from a practical perspective, ingestion of >40 g protein per meal is unlikely to be feasible for the majority of older adults. To address this issue, research has focused on the potential to enhance skeletal muscle protein synthesis rates following the ingestion of ‘suboptimal’ doses of protein via supplementation with specific amino acids such as leucine [29]. For example, it has recently been demonstrated that adding leucine (2.5 g) to a 20 g dose of intact casein protein enhances the specific utilization of dietary protein-derived amino acids for de novo protein synthesis under resting conditions in older men [29]. Furthermore, Dickinson and colleagues recently reported that leucine-enriched amino acid ingestion (10 g EAA; 3.5 vs. 1.85 g leucine) prolonged the duration of the increase in myofibrillar protein synthesis rates following resistance-type exercise in older men [30]. As such, greater doses of protein (~40 g) or slightly lower amounts of high-quality protein fortified with additional leucine may be necessary to achieve a more robust stimulation of post-exercise muscle protein synthesis rates in older adults.

5 Potential Mechanisms Explaining Age-Related Differences in the Dose-Response Relationship Between Protein Ingestion and Skeletal Muscle Reconditioning Following Resistance-Type Exercise

Increases in muscle protein synthesis induced by both resistance-type exercise and protein ingestion are mediated through the mammalian target of rapamycin complex-1 (mTORC1) pathway (for an in-depth review see McGlory and Phillips [31]). Age-related anabolic resistance to dose-dependent increases in amino acid intake [12] and resistance-type exercise [13] have been associated with a reduced p70S6K1^{Thr389} phosphorylation response, suggesting an inability to enhance messenger RNA (mRNA) translation, the rate-controlling step for muscle protein synthesis that is primarily regulated by the mTORC1 signaling pathway [31]. As mentioned in Sect. 4, there have been no direct age-related comparisons on the dose-dependent relationship between protein ingestion and muscle protein synthesis after resistance-type exercise. Of the dose-response studies conducted in older adults [9–11], none measured proteins within the mTORC1 pathway. However, D'Souza et al. [32] demonstrated a dose-response relationship between whey protein ingestion and p70S6K1^{Thr389} phosphorylation up to 40 g of whey protein in the muscle of older men during recovery from resistance-type exercise. Although no measures of muscle protein synthesis were reported, p70S6K1^{Thr389} phosphorylation correlated with intramuscular leucine concentration [32]. Increased leucine intake has also been reported to induce a rapid and prolonged increase in the skeletal muscle mRNA abundance of select amino acid transporters in conjunction with a more prolonged increase in skeletal muscle protein synthesis rates after resistance-type exercise in older adults [30]. Therefore, the capacity of older skeletal muscle to mount a robust protein synthetic response following ingestion of larger doses of protein (~40 g) may relate to leucine-mediated increases in p70S6K1^{Thr389} phosphorylation and/or amino acid transporter expression. However, impairments at the level of anabolic signaling proteins within skeletal muscle may be related to upstream factors such as age-related differences in protein digestion/absorption kinetics [33] and/or postprandial muscle microvascular responsiveness [34], which may alter plasma and intramuscular availability of dietary protein-derived amino acids from ingested protein. For example, we have recently demonstrated that ageing is associated with a relative reduction in the availability of dietary protein-derived amino acids within the circulation following protein ingestion [33]. Through the application of intrinsically labeled (with stable isotopes) dietary

proteins coupled with the use of a primed continuous intravenous infusion of stable isotope-labeled tracer amino acids, it is possible to obtain a traditional measure of postprandial muscle protein synthesis (based on the calculated fractional synthesis rate [FSR]) and more directly assess the metabolic fate of ingested protein-derived amino acids, including the percentage of dietary protein-derived amino acids that appear in the plasma circulation and muscle free pool, as well as their specific use in supporting de novo muscle protein synthesis [35] following resistance-type exercise. Assessing the metabolic fate of dietary protein-derived amino acids in skeletal muscle while also obtaining measures of FSR may provide insight into how efficiently dietary protein-based amino acids from ingested protein are being utilized during post-exercise recovery. As mentioned in Sect. 3, we have previously shown that an acute session of resistance-type exercise prior to protein intake facilitates a greater use of dietary protein-derived amino acids (from the ingested protein) for incorporation into de novo mixed muscle protein in both younger and older men [19].

6 Conclusions and Future Directions

Independent laboratories have demonstrated that ingestion of ~20 g (~0.25 g protein/kilogram bodyweight) of a high-quality protein is sufficient to maximize skeletal muscle protein synthesis rates during recovery from resistance-type exercise in younger adults. However, there is not a clear consensus on the amount of ingested protein required to maximize skeletal muscle protein synthesis rates during recovery from resistance-type exercise in older adults. Even during post-exercise recovery, there appears to be a blunted post-prandial muscle protein synthetic response in older adults when ingesting up to ~20 g protein, with at least 40 g (or ~0.40 g protein/kilogram bodyweight) of dietary protein being required to elicit a robust stimulation of skeletal muscle protein synthesis. There are a lack of data available with which to draw clear recommendations on the amount of ingested protein to maximally stimulate skeletal muscle protein synthesis after resistance-type exercise in younger and older females; this is an area requiring further research. An attractive hypothesis is that resistance-type exercise training and/or increased levels of physical activity can effectively reduce age-related anabolic resistance to protein feeding, thereby increasing the effectiveness of smaller amounts of ingested protein while also reducing the quantity of protein required to induce a robust stimulation of muscle protein synthesis after resistance-type exercise. Additionally, whether older athletes (>65 years)

with above-average fitness levels (i.e. masters athletes) are protected from anabolic resistance will help to unravel the contribution of ageing, as opposed to age-related decreases in physical activity, on the decreases in muscle protein synthesis in response to protein intake, muscle contraction, and their combination commonly observed in older adults. Older athletes and exercisers who employ nutritional strategies that take into account optimal protein intake after exercise, place themselves in a better position to adaptively respond to training, thereby increasing muscle mass and strength, and improving training efficiency in the long term.

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Compliance with Ethical Standards

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