Effect of Protein, Dairy Components and Energy Balance in Optimizing Body Composition

Stuart M. Phillips\textsuperscript{a} · Michael B. Zemel\textsuperscript{b}

\textsuperscript{a}Exercise Metabolism Research Group – Department of Kinesiology, McMaster University, Hamilton, ON, Canada; \textsuperscript{b}The Nutrition Institute, The University of Tennessee, Knoxville, TN., USA

Abstract
Weight loss is achieved through the consumption of a hypoenergetic diet and/or increased energy expenditure through exercise. While weight loss is associated with numerous benefits, the pattern of weight loss in terms of body composition changes is not always studied. In our view, the optimum pattern of weight loss is one in which fat mass is lost and lean mass is preserved. The preservation of lean mass has important consequences due to the role of this tissue in contributing to basal metabolic rate, controlling glycemia, and contributing to lipid oxidation. We also propose that a preservation of lean mass would have important consequences in resisting weight regain after loss. We review dietary practices, including reduced consumption of dietary carbohydrate, consuming higher than recommended dietary protein, with an emphasis on dairy sources, as well as dietary calcium, to accelerate the loss of fat mass during dieting and preserve lean mass. Available evidence suggests that each practice has a highly plausible mechanistic and growing clinical rationale in terms of efficacy in promoting fat mass loss and lean mass retention during a hypoenergetic diet.

Introduction

Obesity and leanness are complex genetic traits, with multiple genes interacting to modulate energetic efficiency, including regulation of lipid storage in adipose tissue and lipid oxidation in support of new protein synthesis in skeletal muscle. However, the metabolic pathways operated by these genetic factors may also be modulated by specific nutrients, foods or dietary patterns, providing opportunities for functional foods and ingredients to alter body
composition independently of their energy content. Weight loss, however, must depend on either reducing habitual energy intake or/and increasing habitual energy expenditure, or some combination of these two options. Many studies have shown the benefits of both approaches alone and in combination to promote weight loss, favorable blood lipid changes, better glycemic regulation, and a host of other benefits. Nonetheless, the longest-term studies on the efficacy of diet-only weight loss programs have reported that most participants regain their lost weight and continue on an upward trajectory in terms of weight gain [1]. A registry of what have been termed ‘successful long-term weight losers’ is now maintained and characteristics of those people are being examined [2, 3]. This review will assess the efficacy of certain dietary practices, alone or in combination with programs of exercise, on people’s capacity to lose weight and more importantly to affect the pattern of weight loss in terms of body composition. The focus on body composition is important because loss of lean as well as fat mass will have both short- and long-term consequences that may affect a person’s capacity to regain weight and affect their metabolic health. The focus of this review is on patterns of dietary macronutrients that appear, at least in short-term studies, to be more effective in promoting loss of fat mass and promoting lean mass retention. We also review the components enriched in dairy, such as calcium, vitamin D (when present as a supplement) and leucine, as important factors in promoting fat mass loss and lean mass retention or accretion.

The relative energy deficit created by dietary energy restriction and/or increased energy expenditure is clearly the primary driver of weight loss, but certain patterns of macronutrients and ingredients might create a generically applicable efficacious approach to weight loss. Dietary patterns may affect the rate and composition of weight loss; however, our recommendations extend beyond the energy deficit. In this review, we focus on weight loss strategies that affect not only the quantity of weight loss but the ‘quality’ of weight loss. An improved quality of weight loss is defined as being the loss of weight with the highest possible ratio of fat to lean mass loss with the further aim to promote loss of as much visceral body fat as possible. We propose that this weight loss pattern is important for short and long-term metabolic health and possibly aids in resistance to weight regain after loss [4–6]. The measurement of weight loss without focusing on the loss of skeletal muscle as a highly metabolically active tissue is flawed. Skeletal muscle is the largest single contributor to basal metabolic rate (BMR) [7] and its loss during a hypoeenergetic period is therefore one of the main reasons why BMR declines with weight loss [8]. A decline in BMR will affect the acute reduction in weight loss and the long-term maintenance of a lower body mass. Weight loss resulting from reduced energy intake will lead to loss of skeletal muscle, which is unlikely to be reclaimed in the absence of resistance exercise to stimulate muscle hypertrophy, resulting in a chronic decline of BMR [9]. Moreover, skeletal muscle is the primary site of postprandial blood
glucose disposal [10], and thus plays an integral role in regulation of glycemia and risk for type 2 diabetes [10]. Also, due virtually entirely to its mass, skeletal muscle is a significant contributor to lipid oxidation and thus is an important contributor to postprandial lipemia [11] and overall blood lipid regulation [11]. In the light of these roles of skeletal muscle and adipose tissue, it is apparent that weight loss strategies need to protect against loss of skeletal muscle and promote fat, especially visceral fat, loss.

**Macronutrient Composition**

The macronutrient composition of energy-restricted diets and the influence of these ratios on weight loss remain somewhat controversial. As recently as 2010 in the Dietary Guidelines for Americans the following conclusion was reached: ‘There is strong and consistent evidence that when calorie intake is controlled, macronutrient proportion of the diet is not related to losing weight’. (http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/DGAC/Report/D-1-EnergyBalance.pdf). An important caveat in this conclusion, however, is in regards to the composition of the weight lost and the failure of the preceding statement to differentiate between the outcomes of subject compliance and diet...
efficacy [1]. The composition of weight loss with energy-restricted diets is generally 70–80% adipose and 30–20% lean tissue (almost exclusively skeletal muscle) [12]. As stated in the introduction, this pattern of weight loss will influence metabolic function during weight loss. The decline in BMR that accompanies weight loss is a primary reason for the slowed rate of weight loss seen in longer-term programs due to a gradual narrowing of the gap between energy requirement for weight maintenance.

Many weight loss diets set protein at 15% of energy, <30% lipids, and 50–55% carbohydrates, with reductions in dietary fat and increases in dietary fiber being favored. It is reasonable to reduce energy density with this ratio of macronutrients and promote weight loss in the short term, but this diet is associated with low satiety and poor long-term adherence [1, 13, 14]. Emerging evidence suggests that reducing the intake of dietary carbohydrates is critically important for promoting both greater weight loss and greater loss of body fat [13–15]. The mechanisms underpinning this effect are uncertain but may relate to a lower daily blood glucose and insulin levels [16]. Insulin’s primary function as a hormone is to promote storage of blood glucose in skeletal muscle and adipose tissue and to inhibit lipolysis and promote triglyceride synthesis and storage [16]. This may explain why a hallmark adaptation to lower carbohydrate diets is a pronounced reduction in circulating triglycerides versus other diets. A proven strategy, and one that is beneficial, is also to reduce not just the total quantity of carbohydrate but also to globally lower the glycemic load of the diet by selecting low glycemic-index (GI) carbohydrate sources [13]. In a weight loss context, such a strategy has been shown to be effective and also results in lowered insulin levels [16] and triglyceridemia [17]. It does need to be highlighted that following lower carbohydrate, lower GI diets may be a problem for endurance athletes seeking to compete since dietary carbohydrate intakes are recommended to be higher to allow full recovery of muscle glycogen stores. While lower total and relative carbohydrate diets appear effective, an important question is what macronutrient should replace the carbohydrate. Diets moderately high (no more than 35% of total energy intake) in protein and modestly restricted in carbohydrate (no less than 35% of total energy intake) and fat may have more beneficial effects on body weight homeostasis and associated metabolic variables [13–17]. Other factors such as dietary omega-3 fatty acids may also be important for weight loss given their impact on satiety and potentially on muscle anabolism. We focus here on moderate-protein diets (30–35% energy at the expense of carbohydrates) and those with low-GI carbohydrates (within the 40% energy).

Increasing protein to higher than the recommended dietary allowance (RDA) levels of 0.8 g protein/kg per day has a beneficial effect on retention of lean mass during hypoenergetic periods of weight loss [13–17]. In fact, in their meta-analysis, Krieger et al. [15] pointed out that in short-term trials (<12 weeks), protein intakes that were 40% higher than the RDA were associated with a 0.60
kg additional fat-free mass retention compared with diets with lower protein intakes. If the trials examined were extended beyond 12 weeks, then this difference grew to a 1.2 kg preservation of lean mass versus lower protein diets. The decrement in lean mass induced by a period of reduced energy intake can also be offset with a resistive exercise component to aid in muscle mass retention [18]. A small handful of studies have also reported that the combination of higher protein consumption and performance of exercise has a synergistic effect in terms of preservation of skeletal muscle mass [18, 19]. An important point is that such a strategy results in less total weight being lost, which may or may not be desirable. A few studies have shown that strength, for example, is preserved during periods of weight loss, and so a consideration for athletes is that if it is weight loss pure and simple that they require then preservation of lean mass may not be concern [20]. However, it is unlikely that such a strategy can continue unabated, and eventually reductions in athletic performance are likely to occur [20]. From the perspective of the metabolic consequences and for the general population, the preservation of lean mass during weight loss would appear of paramount concern.

It is unclear why protein would have a lean mass-sparing effect during weight loss, but it likely relates to the stimulatory effect of protein on muscle protein synthesis (MPS) [21, 22]. The periodic meal-induced stimulation of MPS maintains skeletal muscle mass [21], so it is reasonable to assume that MPS could be stimulated to a greater extent than with a lower protein diet, although there is no direct evidence for this. It is also possible that hypercortisolemia during weight loss would provide a stimulus opposing retention of muscle protein. In men undergoing chronic bed rest with pharmacologically induced elevations in corticoid hormones, a markedly atrophic condition, supplementation with essential amino acids provided some relief against muscle loss [23]. Thus, while it may depend on the extent and duration of the energy deficit and the duration, higher protein diets have been shown to ameliorate loss of lean muscle mass. There may also be a role for higher quality proteins in opposing loss of muscle mass due to the crucial role of leucine in activating the process of MPS and promoting retention of lean mass during hypoenergetic periods [24]. Such a thesis has been proposed and has experimental support in animal models [24], but currently lacks direct experimental evidence in humans. A further extension of this thesis has been provided by Devkota and Layman, who defined the dose of leucine (2.5 g) that is required to stimulate MPS maximally and also provided advice on the meal frequency required to maximally stimulate MPS and thus retain muscle protein [25].

Other mechanisms that have been proposed as to why protein is an effective substitution for dietary carbohydrate relate to protein’s satiety-promoting effects, which appear to be greater than those of carbohydrate and fat. In addition, the thermogenic effect of protein consumption has long been known to be the greatest of all macronutrients.
Role of Calcium and Dairy Components

The original concept of calcium and dairy modulation of body composition and weight management emerged as a surprising finding from a clinical trial evaluating the role of dairy in hypertension, with subsequent corroboration via animal studies, cellular studies to provide a mechanistic framework, secondary analysis of clinical studies originally performed to assess skeletal outcomes and finally prospective clinical trials to assess the effects of calcium and dairy foods on adiposity. In the original hypertension study, isoenergetic substitution of yogurt (454 g/day) in the daily diet resulted in a significant 4.9 kg reduction in body fat [26]. This ‘anti-obesity’ effect of dietary calcium was confirmed in a series of studies conducted in a mouse model of diet-induced obesity (aP-2-agouti transgenic mice [26–28]). These mice responded to low-calcium diets with accelerated weight and fat gain, while high calcium diets markedly inhibited lipogenesis, accelerated lipolysis and fat oxidation, increased thermogenesis and suppressed fat gain with no change in energy intake [26]. Further, when the mice were subjected to modest energy restriction, low-calcium diets inhibited body fat loss, while high calcium diets markedly accelerated fat loss [26–28]; notably, utilizing dairy as the calcium source without altering macronutrient composition resulted in substantially greater effects compared to calcium carbonate.

Dietary calcium and dairy also alter the partitioning of dietary energy during refeeding following weight loss by obese mice [28]. Although post-obese mice fed low-calcium diets exhibited rapid weight and fat regain, increasing dietary calcium prevented the suppression of lipolysis and fat oxidation that otherwise accompanies energy repletion and instead upregulated skeletal muscle fat oxidation [28], reflecting a repartitioning of energy from storage in adipose tissue to oxidation in skeletal muscle. The result is an increase in metabolic rate that is not compensated for by energy intake. As a result, high calcium diets prevented 50–85% of the weight and fat regain found in the animals fed the low calcium diet, with significantly greater effects found with dairy than with elemental calcium [28].

Mechanisms

The anti-obesity effects of dairy foods include both calcium-dependent and calcium-independent mechanisms. The calcium component appears to be mediated by calcium suppression of calcitrophic hormones and by calcium binding to fatty acids in the gastrointestinal tract, forming soaps and thereby reducing fat absorption [29].

Calcitriol (1,25-dihydroxyvitamin D), released in response to suboptimal calcium intakes, stimulates increases in human adipocyte intracellular Ca²⁺, while dietary calcium, by virtue of suppressing calcitriol levels, decreases intracellular Ca²⁺ [30]. Increased adipocyte Ca²⁺ signaling stimulates the expression and activity of fatty acid synthase [27, 31, 32], a key regulatory lipogenic gene,
resulting in increased lipid synthesis. Elevated intracellular Ca\textsuperscript{2+} also inhibits lipolysis, and the combination of increased lipid synthesis and decreased degradation results in an expansion of adipocyte triglyceride storage [33]. Calcitriol also inhibits the expression of uncoupling protein 2 (UCP2) [34], potentially resulting in increased coupling of mitochondrial energy metabolism to ATP production and increasing the efficiency of adipocyte energy storage, while dietary calcium increases adipose tissue UCP2 expression [34].

Human data support these mechanisms. Suppressing calcitriol with high dairy diets increased lipolysis [35, 36] and caused a 30 g/day (270 kcal/day) increase in fat oxidation in a randomized, controlled crossover study under highly controlled conditions using a whole-room calorimeter [35]. Similarly, long-term (one year) consumption of a dairy-rich high calcium diet resulted in increased fat oxidation responses to meal challenges [37].

Rodent and human studies demonstrate a shift in the distribution of body fat loss on high- versus low-calcium diets during energy restriction, with preferential loss of visceral adipose tissue. Excessive central fat deposition in obesity may result from the greater capacity for local regeneration of active glucocorticoids in the visceral fat depot, which is controlled by the activity of 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD 1) to generate active cortisol. Calcitriol directly upregulates adipocyte 11β-HSD 1 expression and cortisol release and, consequently, correspondingly affects local cortisol levels, indicating a potential role for calcitriol in visceral adiposity [38, 39].

**Role of Branched-Chain Amino Acids**

Depletion of calcium from milk reduces its anti-obesity efficacy in rodents, but calcium-depleted milk still retains ~50–60% of the anti-obesity bioactivity of intact milk, most of which can be restored by increasing the branched chain amino acid content of a low-calcium/non-dairy diet to the level found in milk or whey [40]. The abundance of leucine in dairy protein is of particular interest, as it plays a pivotal role in translation initiation of protein synthesis and appears to be important for repartitioning of dietary energy from adipose tissue to skeletal muscle [40–42], see fig. 1.

Leucine coordinately regulates lipid metabolism and energy partitioning between adipocytes and skeletal muscle cells [42] by inhibiting energy storage in adipocytes, and stimulating skeletal muscle mitochondrial biogenesis and fatty acid oxidation [42, 43]. These effects may represent a means of supplying the additional metabolic energy necessary to support this additional protein synthesis [42, 43]. These effects resulted in a 33.4 g/day (300 kcal) increase in fat oxidation in sedentary overweight and obese individuals [44].

**Clinical Data**

Several randomized clinical trials have evaluated the magnitude and significance of this effect in humans. In the initial trial [45], 32 obese adults were maintained
on balanced energy deficit diets (500 kcal/day deficit) and randomized to control (0–1 serving/day and 400–500 mg Ca/day supplemented with placebo), high-calcium (control diet supplemented with 800 mg Ca/day), or high-dairy (3–4 servings of dairy foods, primarily milk, total Ca intake of 1,200–1,300 mg/day) diets. The high-calcium diet augmented weight loss by 59%, and the high dairy diet increased it twofold. Fat loss followed a similar trend, with the high-calcium and high-dairy food diets augmenting the fat loss found on the low-calcium diet by 38 and 64%, respectively. This was accompanied by a marked change in the distribution of body fat loss; central (trunk) fat loss represented 19% of the total fat lost on the low-calcium diet, and this was increased to 50 and 66% of the fat lost on the high-calcium and high-dairy diets, respectively [45].

These findings were confirmed in several follow-up randomized clinical trials in Caucasians and African-Americans under conditions of modest energy restriction, and one multi-centre trial with a similar experimental design [46, 47]. In the absence of energy restriction, dairy exerts little effect on body weight but still exerts significant effects on body composition. In the absence of energy restriction, increasing dairy intake resulted in a 5.4% reduction in total body fat and a 4.6% decrease in trunk fat (p < 0.01 for both) without any change in body weight while a control group maintained on a low-calcium/low-dairy diet with identical macronutrient composition exhibited no significant changes in total body fat or trunk fat [46]. Data from two long-term large-scale placebo-controlled double-blind intervention trials further support a significant role for calcium in improving adiposity in the absence of energy restriction [48, 49]. This modulation of adiposity by dietary calcium exhibits a threshold effect. Major and colleagues recently demonstrated a highly significant 6 kg weight loss in obese women with low baseline calcium intakes (<600 mg/day), while those consuming higher levels of calcium did not exhibit this effect.

Two studies [50, 51] utilizing a similar design to those noted above [36, 52] found no effect of dairy during energy restriction, but subjects in the higher dairy group in both studies consumed significantly more energy (150–200 kcal/day) than was consumed by subjects in the low-dairy control groups, suggesting that the dairy may have permitted greater energy consumption without adversely affecting body weight. Other clinical trials also support a role for dairy or dairy components in weight management. Whey supplementation resulted in significant augmentation of fat loss accompanied by increases in lean mass in previously sedentary exercising individuals [53] as well as individuals subjected to an energy deficit [54]. Similar effects have been noted in studies of weight regain following energy restriction [55, 56].

Although most clinical trials to date have been conducted in adults, a recent 6-month trial of 120 obese primary school-aged (5.6 + 0.5 years) children with a 3-year follow-up [57] demonstrates that dairy-rich diets contribute significantly to successful weight management, manifested as significant effects on BMI and waist circumference over a 3-year study period.
These effects are also supported by a number of observational studies reporting an inverse relationship between dairy foods and/or dairy components and either body weight or body fat in multiple population groups, including children, young adults and older adults of multiple ethnicities [for a recent review, see 58]. Similar inverse relationships have also been reported in multiple epidemiological studies [58] and secondary analyses of clinical trials originally conducted with other end points [59, 60].

**Conclusion**

The energy gap between intake and expenditure is the primary determinant of weight loss, but quantitatively minor components may play a major role in weight maintenance in the face of significant daily variation in energy balance. Moreover, focusing only on body weight and not body composition is a flawed approach. Skeletal muscle is the largest tissue contributor to BMR and its preservation is important. Skeletal muscle also plays a large role in postprandial glycemic regulation and lipemia, which highlights the importance of its preservation during weight loss. Thus, hypoenergetic ‘strategies’ that promote lipolysis and fat mass loss, especially loss of visceral body fat, and incorporate approaches to preserve muscle mass would be desirable over those that blithely address weight loss without regard for composition of that loss. Evidence strongly suggests that certain approaches to weight loss can achieve this pattern. First, fat mass loss is accelerated with a reduction in carbohydrate intake from the population average intake of 55–60% of total energy intake to 40% or less, with particular emphasis on low GI carbohydrates. The main reason for this recommendation has to with maintaining a low systemic insulin concentration, which is a markedly anti-lipolytic hormone. Second, dietary protein would need to be consumed in quantities far higher than the RDA level, making up at least 25–35% of the total hypoenergetic intake. In addition, high-quality proteins rich in branched-chain amino acids, especially leucine, stimulate lean mass retention and fat mass loss. The potential satiety value of protein and the thermogenic response associated with its consumption are further reasons to emphasize the substitution of protein for carbohydrates. Third, calcium intake should be at or above the current adequate intake level of 1,000–1,200 mg daily. Calcium consumption has well-established effects on lipid accretion, lipolysis and oxidation as outlined above, and may have as yet unappreciated effects on appetite and on increasing fecal fat excretion, both of which would enhance the impact of a hypoenergetic diet. Finally, dairy is a good source of two of the highest quality proteins, casein and whey, which are both rich sources of leucine. Dairy is also rich in calcium and other nutrients, which make it an excellent functional food to consume in line with the recommendations above.
References


Dr. Zemel: I’d like to see us bring back the issues related to performance for just a minute. As you pointed out, when you lose weight, about 30% of what you lose is lean mass. However, overweight people have significantly more lean mass to begin with, as a result of moving their extra weight through their activities of daily living. So, using the strategies that you have described, including higher protein, lower carbohydrate and higher dairy to retain lean mass while losing body fat, would you suggest that post-obese individuals who have successfully gone through a program like this might have improved performance as a result of greater lean mass when compared to individuals who maintained their ideal body weight throughout?

Dr. Phillips: The body weight change in our IDEAL study, was lowest on the high dairy protein group because they gained muscle as they lost fat, so the net weight change is about 100% fat loss, and I agree with your point. Whether performance correlates with that, I can’t say. However, many of these very big people cycle through repeated weight loss programs, with loss of skeletal muscle mass each time, and they never fully reclaim...
it back. As a result, their resting metabolic rate begins to decline and they have an even
tougher time losing weight.

Dr. Zemel: When we are talking about macronutrients, as we have up until now, it's
very easy to keep in mind that we are talking about nutrition. When we start talking
about micronutrients, whether we are talking about leucine or calcium, there is a
tendency to forget that we are talking about nutrition and attribute a degree of magical
pharmacology to the micronutrient that we are talking about, which brings me back to
the nice comments you gave about the work from Angelo Tremblay's lab in which he
showed a much greater effect in those with low calcium levels as opposed to those who
had fully replete levels of calcium intake. This may not be a calcium-sensing issue but
instead simply that you are correcting a suboptimal intake.

Dr. Phillips: Interestingly, he reported a similar phenomenon when women were
given a multivitamin during a weight loss program, so maybe it's because they had a
poor dietary pattern to start with and that this correction can improve their weight loss
pattern. So, I am in full agreement, but I struggle with that from a mechanistic
standpoint.

Dr. McLaughlin: We should remember that the gut is a nutrient-sensing organ and
the gut endocrine system plays a big role in satiety. There is some recent evidence
suggesting that the same calcium receptor that's expressed in the parathyroid may also
be expressed in gut endocrine cells, so the gut should be able to sense the luminal calcium
content.

Dr. Lang: I am puzzled about vitamin D. We have just learned that 1,25(OH)\textsubscript{2}D
stimulates calcium entry and that this inhibits lipolysis, yet you add vitamin D to milk
which would increase 1,25(OH)\textsubscript{2}D.

Dr. Phillips: No, what we add is vitamin D\textsubscript{3} (cholecalciferol), the same fortified form
of vitamin D that is in the milk. It doesn't change the active metabolite (1,25-dihydroxy-D)
levels.

Dr. Zemel: Remember that most North Americans have either deficient or suboptimal
levels of vitamin D as measured by 25-hydroxy vitamin D levels. The other thing is that
below 30 ng per ml as you increase dietary vitamin D and increase 25-hydroxy vitamin
D you feed back on PTH and lower PTH levels, so those higher levels of 25-hydroxy
vitamin D lead to a reduction, not an increase, in 1,25-D, so it's a paradoxical decrease.

Dr. Phillips: I didn't show data here, but we conducted a study over 18 months, and
we found that while these women were not deficient, they were definitely not fully
sufficient. This is a grey zone, and may be a conundrum for the dairy industry to talk
about dairy being a good source of vitamin D because the level of fortification of dairy
products in Canada is such that 3 servings gives you 200 IU of vitamin D which is the
current recommended intake. However, this may be 5- to 10-fold less than it should be
(1,000 or 2,000 IU), and even with 6 servings of dairy those women were getting only
about 450 IU of vitamin D. But the parathyroid hormone levels went down in the high
dairy group, although we saw no change in 25-hydroxy-D.

Dr. van Loon: Do the glucocorticoids stimulate calcium entry in adipocytes?

Dr. Zemel: I don't know if I can answer the question of whether they stimulate
calcium entry, but the adipocyte does have an 11-β-hydroxysteroid dehydrogenase, so it
does make its own cortisol. This is an odd relationship between glucocorticoids and
1,25(OH)\textsubscript{2}D, with a feed forward mechanism between the product of 11-β-HSD
(cortisol) and the vitamin D receptor in the adipocyte. So 1,25 D stimulates 11-β-HSD
to produce cortisol, cortisol then upregulates the vitamin D receptor in the adipocyte with this positive feedback. That's not a direct answer but that's as much as I know.

Dr. Hawley: With those elderly or aging women, you find an alteration of muscle mass loss, so what happens in athletes who want to lose fat mass while retaining a high energy expenditure, with protein intake in excess of 50% of dietary energy? Would you expect supplementation with dairy to have any effect on maintenance of muscle mass during energy restriction in athletes under these conditions?

Dr. Phillips: Correcting low calcium intakes will probably result in a loss of more fat mass in those athletes. The retention of lean mass comes from a combination of two signals: provision of protein at regular levels, and resistive/weight-bearing exercise. While those in the high dairy protein group gained lean mass, we found that the women that gained the most lean mass lost the least amount of fat mass. My interpretation of that is that they were the ones who did not comply with the diet, so the closer you get to energy balance or energy surfeit, the more lean mass you gain, it makes sense. What you can't get are absolutely huge changes; a trainer reported he gained 15 pounds and he lost 15 pounds of fat, but I don't believe it. I think you can shift it a little bit, and so I think you can do it in athletes, but the closest we have is the data from the novice trainers in our milk study in terms of their body composition and then the women in that situation.

Dr. Hawley: The difference is that their total protein intake is still way beyond what is needed. In the endurance-trained athlete with an energy intake of 15 or 17 MJ per day who tries to reduce fat mass, further increasing protein content doesn't seem to be physiologically relevant. So, what would you advise for an athlete? To lose the least amount of muscle mass during periods of energy intake restriction?

Dr. Phillips: Our women in this study ended up with around 1.6 g of protein per kg per day, which is twice the RDA. Most endurance athletes, even at 15% protein, come close to these intakes because of their large energy expenditure, but what becomes more important is then the timing of the protein intake. Small amounts of protein immediately after exercise might prevent that catabolic loss of muscle.

Dr. Gibala: Your data are very important because many people believe that exercise stimulates AMPK, which feeds back to inhibit mTOR; a little bit of protein apparently will overcome that.

Dr. Baar: I don't think that there is any doubt that AMP kinase and mTOR activity can go up at the same time. It only becomes an issue when you get to the elite level, where small changes make the difference: there it becomes an issue, but it is not important for average people. In extreme conditions where you use proper nutrition, the mTOR interaction is minimized.

Dr. Hawley: The IDEAL study data are very compelling and it’s interesting to know that the ratio of energy restriction to exercise was heavily biased towards restriction of energy intake.

Dr. Phillips: What I initially wanted to do was to have these women come in 5 days a week and walk around our indoor track at a specified pace. However, my graduate student said we have to give them some flexibility, so we gave them a device called the body media armband that senses skin temperature, heat flux, and has a bi-axial accelerometer and that’s programmed to count 250 cal; it counts down and it’s a great feedback, but it’s independent of exercise. I agree with you and would have liked to have gone a little bit heavier in terms of the exercise, but we were very worried about
adherence. In retrospect, adherence to the diet was not good while the adherence to the exercise was exceptional. The women in the high dairy group gained more strength in a few selected exercises; they didn't gain much strength, as they were training only two days a week, but it was greater in that group. In an athletic population you could probably hit the exercise harder, but the dietary restriction tends to contribute to the fat loss. I do think that the reduction in carbohydrate at the right phase of their training cycle is important for mediating fat loss.

Dr. Gibala: Do you think that adherence to the diet will continue? I know some individuals found the high dairy diet to be tough.

Dr. Phillips: With 90 women from diverse ethnic backgrounds, we expected some lactose intolerance, and 46 women came into the study and said they were lactose intolerant. However, only one woman had to drop because of GI symptoms, so lactose intolerance was not a big issue. At the end of the study, we gave them an enormous questionnaire to ask them to rate their perceived adherence to the diet: we knew their exercise adherence because they had to come in to the gym to train. We did look at some body image issues, and the differences between the diets were fairly small, but the exercise efficacy, what they felt they could do, was greatly enhanced. The diet not as much, but they definitely felt they could stick with the exercise after this.

Dr. Haschke: A short comment on milk protein. We had a Nestlé Nutrition Workshop on the value of milk because the company is probably the biggest producer of milk in the world, so we have a high interest in the value of milk. A group from Frankfurt and Offenbach showed that milk protein per se has a very unfavorable insulinogenic index. It stimulates insulin secretion more than all other reference proteins used. They showed in animal experiments that this is a predisposing factor to insulin resistance, and they have good epidemiological data now that this might be associated in risk groups, those who are obese, with the development of type 2 diabetes. There was a response from another group from Puna, India, where 40–50% of people have diabetes type 2 and their protein source is milk because in that area people are 70–80% vegetarians, so their only protein intake from animal sources is milk. If you are proposing very high intake of milk protein for at-risk groups, I think they should be evaluated first.

Dr. Phillips: I completely dispute that data. The most recent meta-analyses have actually shown that it's entirely the opposite, that consumption of milk in dairy products actually reduces the incidence of type 2 diabetes and reduces the incidence particularly of metabolic syndrome, and so I am not sure that I put any stock in those data.

Dr. Haschke: I am neutral because I just report here what was said and has been published. The fact that the milk protein is more insulinogenic than the other ones is clear: this cannot be disputed. The other things, the long-term effects, I agree with you, this has to be shown.

Dr. Phillips: The consensus on this is that the health benefits of milk and dairy consumption are far from negative; so, as an isolated protein I would agree with the insulin response, but in the context of consuming dairy products as a food, there is no difference, and so if I wanted to compare the insulin response of consumption of milk with consumption of a soft drink, for example.

Dr. Haschke: This is a different story, one is protein and the other one is carbohydrate. I am just focusing on the protein quality. Excess of one protein might not be so good, but in balance I think it's adequate and should be consumed. Nobody is against milk for the
healthy population, but I just wanted to bring this up as a caveat that we should not go in one direction without being sure.

*Dr. van Loon:* We should also look at the mechanism. We spent 10 years in looking at how to optimize the insulinotropic response of amino acids and specific proteins. Proteins with a high leucine content which are easily digested and absorbed give a very high insulin response, especially when coingested with carbohydrates. If you add protein or add the right protein to each meal, you actually get a greater glucose disposal capacity and a reduced glycemic response; we have done this and improved glycemic control in diabetics, for example.

*Dr. Haschke:* Glycemic control is no problem: milk has a very low glycemic index, but it has nothing to do with the insulinogenic index.

*Dr. van Loon:* But if you take a glass of milk with a high carbohydrate meal your subsequent glycemic response will be improved simply by stimulating the insulinotropic potential of the meal, and that is advantageous.

*Dr. Zemel:* Milk protein by itself is an insulinotropic agent, without a doubt, but when you substitute milk protein for other proteins in a meal while keeping macronutrients constant, insulin resistance index actually goes down. This was reported in both cohort and randomized clinical trials. For example, 10-year data from the CARDIA study show each of the elements of the insulin resistance syndrome going down, including an improvement in insulin sensitivity.

*Dr. Haschke:* Are these effects from milk and milk proteins?

*Dr. Phillips:* It is dairy products. That's the whole point; it's part of an entire diet. In fact, if you want to talk about the glycemic load of the diets, they are about the same, but I can tell you that the insulin sensitivity index in the high dairy protein group improved the most.

*Dr. Montain:* The military have a different challenge. Soldiers go out on a patrol and are moving about so much that it's hard to get enough food so they tend to lose weight during that period of time; then they come back to the base and have a chance to recover. But often they lose weight and they complain that they have lost strength and ability to work. Evidently, their recovery time is not long enough or they eat poorly during that period of time. What strategy would you recommend?

*Dr. Phillips:* My understanding is that soldiers practice all kinds of dietary habits, with some eating rushed throughout the day in small amounts, and some sitting down to eat all at once. Obviously, we would advocate for a good percentage of their energy coming from protein and lower glycemic index carbohydrates as opposed to coming from simple sugar. From the standpoint of when they should eat and how often, it comes back to an optimal strategy of consuming a bolus of protein close to 20 g at a time. Outside of that, I am not sure I can do much more. Obviously, they have got a lot of other things going on, and I am not so sure that the loss in strength that they talk about is as much lean mass loss as it is a psychological issue, but maybe that's something from a neurotransmitter standpoint that is mediated by protein as well.

*Dr. Montain:* What about their recovery then?

*Dr. Phillips:* There are three masters you have to serve: rehydration, glycogen restoration and repair and adaptation. If you feed a soldier, I don't know whether adaptation is important but definitely repair for a damaged muscle or ligaments requires some substrate. I don't know what the optimal prescription is, but it would certainly be similar to an athlete. If it's practical, they should eat as soon as possible, because recovery starts from there.
**Dr. van Loon:** If people switch to high protein intake over short periods of time and then switch to very low energy intake, you don’t adapt to the situation and that could also cause a massive lean muscle mass loss; nobody has really looked at that, but if you increase protein intake to a very high level for a few weeks and then immediately close it down again you get a different situation.

**Dr. Phillips:** I think that might be one of our issues.

**Dr. Maughan:** Elite strength-trained athletes who have qualifying competitions and eat very high amounts of protein up to those qualifying competitions tell us that when they then ease off, they lose enormous amounts of muscle mass in the space of a week or two. This fits with Joe Millward’s adaptive metabolic demands model, because they have gone from enormously high protein intake to a relatively normal intake.

**Dr. Phillips:** If you want to preserve muscle mass, you have got to wean yourself off of a high protein intake, there is no question about that. We are talking about consuming protein here probably over and above what we could be able to put into the muscle, and there is no question but it’s acting as a satiety signal in a lot of these situations too.

**Dr. Burke:** What about populations that are athletic or happy to do more exercise than the 250 cal a day; if they are hypoenergetic and want to have a high protein intake, given the insulinenic protection with dairy protein, would you sacrifice some fat and allow more carbohydrate intake so that you have got more fuel requirements replaced?

**Dr. Phillips:** If you are going to cut down carbohydrate, it’s either protein or fat replacement.

**Dr. Burke:** But if you preserve the protein, could you sacrifice some fat and keep the carbohydrate high and allow more fuel replacement?

**Dr. Phillips:** Maintaining protein intakes would aid adherence to the diet, because the protein is an important satiety signal.

**Dr. Burke:** I am keeping the protein the same. I am wondering if it’s just fitting around the carbohydrate and if all dairy is the same, and so if are you thinking about cheese or milk where you have got casein versus the whey components, are we going to see the same effect?

**Dr. Phillips:** The 6 servings of dairy here were 4 servings as fluid skim milk, two of them chocolate flavor, 3 small yoghurts, each as a half serving and a serving of cheese, so it was just dairy but with no attention paid to one type or the other. I don’t know whether you get something different from each different type. However, there is difference in satiety signals that come from fluids as opposed to solids, so we thought that it was better to mix it up.

**Dr. Burke:** If you talk about dairy, is cheese the same as milk and yoghurt?

**Dr. Zemel:** In our animal studies, we isolate the non-calcium bioactivity to whey, so I wouldn’t expect equal benefit from cheese. We have never done a study with cheese only, but where we have given 3 or 4 servings of dairy per day, we would never allow more than one of those servings to be cheese simply because I was concerned about stripping the whey out of the diet. Obviously, when we use milk and yoghurt, we have both the casein and the whey present. So, while we don’t have clinical data to answer your question, our animal data indicate that cheese is not the same.

**Dr. Maughan:** It is well recognized in the farming business that high protein diets are good for weight loss. Cattle with a bit too much fat have difficulty calving, but putting more protein in the feed for 2 weeks can result in a weight loss of 20–30 kg, almost all of it fat. Maybe we can learn something from the farming world.