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#### QUESTION

#### 1. What Do You Understand By The Term "Biological Value Of Proteins?"

The biological value of a protein extends beyond its amino-acid composition and digestibility, and can be influenced by additional factors in a tissue-specific manner. In healthy individuals, the slow appearance of dietary amino acids in the portal vein and subsequently in the systemic circulation in response to bolus protein ingestion improves nitrogen retention and decreases urea production.

This is promoted by slow absorption when only protein is ingested (e.g. casein). When a full meal is ingested, whey achieves slightly better nitrogen retention than soy or casein, which is very likely achieved by its high content of essential amino acids (especially leucine). Elderly people exhibit 'anabolic resistance' implying that more protein is required to reach maximal rates of muscle protein synthesis compared to young individuals. Protein utilization in inflammatory or traumatic conditions increases substantially in the splanchnic tissues containing most of the immune system, and in wounds and growing tissues. This happens especially in the elderly, which often suffer from chronic inflammatory activity due to disease, physical inactivity and/or the aging process itself. Consequently, the proportion of protein absorbed in the gut and utilized for muscle protein synthesis decreases in these situations.

This compromises dietary-protein-induced stimulation of muscle protein synthesis and ultimately results in increased requirements of protein ( $\sim$ 1.2 g/kg body weight/day) to limit gradual muscle loss with age. To optimally preserve muscle mass, physical exercise is required. Exercise has both direct effects on muscle mass and health, and indirect effects by increasing the utilization of dietary protein (especially whey) to enhance rates of muscle protein synthesis.

What are high biological values of proteins?

Animal sources of protein are meat, poultry, fish, eggs, milk, cheese and yogurt, and they provide **high biological value proteins**. Plants, legumes, grains, nuts, seeds and vegetables provide **low biological value proteins**.

### QUESTION

# 2. LIST AND EXPLAIN THE VARIOUS METHODS OF ASSESSMENT OF PROTEIN QUALITY

#### 1. BODY PROTEIN METABOLISM

#### 2. DIETARY PROTEIN AND AMINO ACID BIOAVAILABILITY

## 3. . PROTEIN QUALITY IN RELATION TO ENERGY TURNOVER AND GLUCOSE HOMEOSTASIS

#### **1. BODY PROTEIN METABOLISM**

Assessing protein quality with respect to its efficiency in supporting body protein metabolism should include consideration of the capacity of the diet to provide substrate needs for protein synthesis and any other biosynthetic pathways, i.e., a suitable source of nitrogen and IAA (lysine, threonine, valine, isoleucine, leucine, methionine, phenylalanine, tryptophan, and histidine). However, to this assessment method should be added provision of sufficient signal amino acids, (e.g., leucine), required for those regulatory steps whereby metabolism is optimized and anabolism is stimulated. It is arguable that current methods used for assessing protein quality have only evaluated substrate needs rather than any provision of regulatory amino acids.

Evaluation of protein quality with the PDCAAS approach measures the protein's metabolic effectiveness at a dietary intake that meets minimum requirements. By this measure, protein requirements are low compared with most nutritionally complete habitual diets. Indeed, applying an adaptive metabolic demand model of protein homeostasis, protein requirements may be even lower after complete adaptation to the extent that a dietary recommendation based on the true minimum intake for nitrogen equilibrium would become of questionable nutritional significance.

Furthermore, in the context of an adaptive model and the higher habitual protein intakes in subjects consuming the currently recommended healthy diet, it has been suggested that the assessment of protein quality by amino acid scoring becomes problematic, with the metabolic demand for amino acids reflecting a complex adaptive response to varying intakes of protein and amino acids. This means that as protein intake increases, for example toward the upper half of the current acceptable macronutrient density range, both the metabolic demands for amino acids and the consequent fate of the dietary amino acids will become increasingly difficult to predict in terms of generating a single reference amino acid pattern against which to judge protein quality, especially across the entire life span and in all physiologic conditions. For example, leucine regulation of muscle protein synthesis via the mammalian target of rapamycin signal cascade requires increases in intracellular leucine concentration, which also increases amino acid oxidation. The PDCAAS approach argues that increased amino acid oxidation reflects inefficient use of amino acids, but this ignores any transient signaling influence of specific amino acids before their oxidation. Thus, within the context of potential benefits associated with higher protein intakes, it is important to consider to what extent the quality of the protein (e.g., amino acid profile) influences its anabolic signaling.

Although concern has always been expressed about the importance of dietary protein for the elderly, especially in the context of the age-related loss of skeletal muscle mass (sarcopenia), there has not been a firm consensus that the published evidence indicates any measurable age-related change in the minimum protein requirement or the nitrogen-balance data which form the basis of the current PDCAAS reference pattern. However, emerging experimental evidence suggests that there is an age-related change in the regulatory influence of IAA on muscle protein synthesis that will reduce the effectiveness of dietary protein to maintain muscle mass.

Muscle growth and maintenance occurs in response to a complex interplay of stimuli, including physical activity, hormonal signaling, and substrate supply. However, amino acids are a prerequisite for muscle protein synthesis, and a dietary supplement of IAA is a potent stimulus. There is, in fact, a dose-response relation between IAA concentrations in the blood and muscle protein synthesis. In the elderly, there is, at the same time, decreased sensitivity and responsiveness of muscle protein synthesis to IAA. Currently, human studies have not identified the mechanisms of these effects. Although intervention studies point to the need for a combination of both nutritional support and resistance exercise, the ideal amino acid pattern of the extra protein involved is unknown.

There is limited evidence to date on the relative influence of different protein sources on increasing muscle mass in human trials. Studies measuring the effects of meat-containing and lactoovovegetarian diets, coupled with resistance training protocols, on muscle mass have been mixed, although methodology varied and the research is only beginning to emerge. According to Wilkinson et al, fluid skim milk promoted greater muscle protein accretion than a soy protein beverage when consumed after resistance exercise. Phillips et al have suggested that any improved nitrogen retention observed with milk compared with soy consumption during a resistance training protocol may reflect differences in the amino acid profile during delivery to peripheral tissues. However, it is not known whether this is a function of different rates of digestion, peak postprandial amino acid flow through the splanchnic bed and consequent rates of amino acid oxidation and deamination (higher for soy than milk protein), or the different amino acid profiles of the 2 protein sources.

Although human evidence is beginning to emerge, there is abundant evidence from animal studies that sufficiently high doses of leucine may be particularly important in muscle protein synthesis through synergistic effects with insulin in signal transduction pathways and in the presence of adequate dietary energy. As proposed by Garlick, there are worthwhile research opportunities regarding the promising potential role for leucine in protein metabolism as well as the possibility of an intake threshold at which overstimulation by leucine could negatively impact glucose metabolism. A review of the leucine literature by Layman estimated that stimulation of muscle protein synthesis would be optimized with 18 g IAA, including 2.5 g leucine, at each of 3 meals per day.

A clear research goal is to identify the optimal dietary amino acid pattern in terms of specific amino acids, the total IAA content, or perhaps even the conditionally indispensable amino acid for determination of protein quality. Although leucine is abundant in a variety of protein sources,

confirmation of the need for particularly high intakes of leucine at each meal, particularly within a calorie-restricted diet, could have implications for choosing a protein source (Table 1).

#### TABLE 1

Leucine and BCAA content of foods

	Leucine	BCAA
Whey protein isolate	14%	26%
Milk protein	10%	21%
Egg protein	8.5%	20%
Muscle protein	8%	18%
Soy protein isolate	8%	18%
Wheat protein	7%	15%

1. Values reflect g amino acids/100 g protein. BCAA, branched-chain amino acid.

#### 2. Adapted from Layman and Baum.

#### 3. Source: USDA Food Composition Tables.

In addition to muscle, bone is also an important target for anabolic influences of dietary protein. In a rat model there is a clear dose response of bone length growth to protein intakes in excess of those associated with maximal muscle growth, with dietary protein-induced changes in proteoglycan synthesis rates in rat skeletal muscle and bone linked to changes in plasma and tissue insulin-like growth factor-I levels. This is consistent with more rapid catch-up growth in height in children with increased dietary protein intake (15% compared with 7.5% energy), which was associated with higher serum concentrations of IGF-I. Also in relation to the adult bone, it has been argued that dietary proteins enhance IGF-1, a factor that exerts positive activity on skeletal development and bone formation, and are as essential as calcium and vitamin D for bone health and osteoporosis prevention. Although there is no consistent evidence to suggest differences in dietary protein sources on such influences, it is of obvious importance to establish how the amino acid pattern of the protein supply influences such responses not only at the level of the osteocyte but also in terms of IGF-1 production.

#### 2. DIETARY PROTEIN AND AMINO ACID BIOAVAILABILITY

A second important issue in quality evaluation relates to the bioavailability or digestibility of a protein or the capacity to provide metabolically available nitrogen and amino acid to tissues and organs. The food matrix in which a protein is consumed can have significant impact on the bioavailability of amino acid for metabolic needs. Digestive losses and structural changes of amino acids are caused by numerous anti-nutritional factors in foods. These issues have been addressed with particular attention to animal compared with plant proteins.

As mentioned previously, the PDCAAS value is calculated by first scoring the test protein against an appropriate reference amino acid pattern, then correcting for digestibility. The currently accepted method for assessing digestibility is based on measures of fecal nitrogen in a rat assay. Fecal measures in this assay appear to appropriately assess human nitrogen digestibility. It has been noted, however, that ileal measures may better assess amino acid digestibility. Both cost and time involved in measuring true ileal digestibility in human subjects are intensive, although other monogastric species, such as the pig, have been considered. It has also been noted that research is needed to assess the impact of kinetic differences between proteins in the intestinal lumen when measuring ileal digestibility. Sarwar and Schaafsma have argued that digestibility factors developed from the rat bioassay may not appropriately correct for the range of anti-nutrient effects in the food matrix, both naturally occurring and formed through processing methods. Although heat, oxidation, and other treatments are carried out for consumer protection and benefit, they can lead to formation of Maillard compounds, oxidized sulfur amino acid, D-amino acids, or crosslinked peptide chains, which limit amino acid bioavailability.

The multiple anti- nutritional factors present in foods have led Sarwar and Schaafsma to also question the biological efficiency of complementation of low-quality with high-quality proteins. Also, as stated above, the truncation procedure and the restriction to only the first limiting amino acid are subject to criticism because these latter issues do not allow expression of the power of a high-quality protein to balance the IAA composition of inferior proteins.

A high ileal digestibility of proteins is also relevant for reducing the amount of dietary nitrogen entering the colon. Protein fermentation by the intestinal flora may result in the formation of toxic compounds, including ammonia, di hydrogen sulfide, indoles, and phenols that could irritate the colonic epithelial cells and increase the risk of colon cancer.

### **3. PROTEIN QUALITY IN RELATION TO ENERGY TURNOVER AND GLUCOSE HOMEOSTASIS**

Dietary protein function is not usually considered in relation to energy status and glucose homeostasis. Although energy intake and expenditure, either above or below metabolic needs, influences protein utilization, the impact of protein quality in populations with varying levels of energy turnover has not been considered in the past. However, it is logical to question the influence of energy turnover on amino acid needs and the consequent reference amino acid pattern for assessing protein quality in any target population. Current evaluation of dietary protein utilization, especially in relation to its quality, assumes subjects are in energy balance, consuming nutritionally adequate diets, and engaging in moderate rates of physical activity. Departure from energy balance markedly changes protein utilization and has been suggested as an important factor in the lack of reproducibility of the nitrogen balance studies. In subjects who are otherwise in energy balance, the protein utilization effects of varying levels of physical activity are very poorly understood.

In the context of the obesity epidemic, there is an important potential role for protein as a part of diets aiming to limit weight gain or help with weight loss. Several mechanisms have been proposed to explain the well-documented influence of dietary protein's role in body weight regulation, such as thermogenesis, improved body composition, improved glycemic control, and, as discussed below, appetite regulation. These effects have been assumed to relate to the quantity of dietary protein and its relative proportion compared with the other macronutrients. However, there is evidence to suggest mechanisms that would have implications for protein quality assessment.

Improved glycemic control is important in the context of management of type 2 diabetes and also in relation to body-weight regulation. Studies that have increased protein intakes at the expense of carbohydrates have shown that a diet with 30% of energy derived from protein, 20% from carbohydrate (with low biologically available glucose), and 50% from fat is effective in improving glycemic control in people with type 2 diabetes without an adverse effect on serum lipids or renal function. There are several potential mechanisms of these influences of protein which might be responsive to the protein structure or amino acid profile. One is the influence of variation in amino acid composition on the magnitude and duration of postprandial insulin secretion, an important but relatively unexplored question in this context. Another is gluconeogenesis rates in relation to both the pattern of amino acids as substrates as well as their influence as regulators of the metabolic pathway. Individual amino acids differ as substrates for gluconeogenesis, and the branched-chain amino acids have a unique role in providing amino groups for production of alanine (from pyruvate) and recycling of glucose carbon from skeletal muscle to liver for gluconeogenesis.

The overall significance of protein or the amino acid pattern on glucose homeostasis through insulin secretion, de novo glucose production, or alanine recycling has not been investigated