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Human protein requirement: policy issues

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For most of the population of the world plants provide the main dietary source of proteins for consumption (Jackson & Margetts, 1993). Were there to be an absolute need to consume animal protein in order to achieve optimum health, this need would have very considerable implications for food security. Animal protein is expensive to produce in terms of human effort, resource consumption, land use, water and energy requirements. If there is an absolute need for animal protein consumption at even modest levels, it is unlikely in the short to medium term that self-sufficiency can be achieved (Waterlow *et al*. 1998). On the other hand, there is evidence that high levels of consumption of protein can lead to adverse effects, especially during pregnancy, and may accelerate the ageing process, although the evidence for and against there being an increased risk, or rate of disease progression, with higher patterns of consumption is not conclusive (Hu *et al*. 1999; Jackson, 1999*a*,*b*; Millward, 1999*a*,*b*).

Dietary proteins have a physiological function in their own right during breast-feeding, but at all other times dietary proteins are used by the body as a source of amino acids, although they may be better absorbed as di- and tripeptides. Amino acids taken in the diet and formed in the body are utilised to satisfy the body's needs for individual amino acids for protein synthesis and other metabolic pathways. However, our understanding of the quantitative and qualitative demands by the body for individual amino acids is incomplete, and we have to make judgements based on a broad appreciation of the pattern of amino acids which the body needs. Thus, there is a great deal of work to be done in developing a sharper characterisation of the needs for each amino acid by age, gender and physiological and pathological state. This is the basic information which is required in order to determine the amount and pattern of dietary protein which best meets the needs of the body. In the absence of this information all other approaches to determine protein requirements have been based on indirect methods or broad generalisations about the response to the provision of different patterns and amounts of amino acids in the diet.

Dietary reference values and recommended daily amounts

The recommendations on the amount of protein which should be available for the population are based on estimates of the requirements of individuals and groups of individuals (Food and Agriculture Organization/World Health Organization/United Nations University, 1985). The history of the use and development of recommended daily amounts in some form goes back many years, and was originally based on the need for planning purposes. Most usually this need was in the context of famine and hardship, and the primary purpose was to provide a reasonably objective assessment of the amount of food which would have to be provided in order to satisfy the needs of the population, to sustain life at the most basic level: 'a survival standard with an economic background' (Leitch, 1942). At a later stage the objective was changed to provide enough food to enable a work force to achieve and maintain its productivity. It is only relatively recently that the objective has been explicitly to maintain health, or provide 'optimum nutrition'. However, there has always been a degree of debate and controversy about the nature, characterisation and objective of the values (Hollingsworth, 1984; Harper, 1987). It is perhaps a little alarming that we have not been able to find a form of words which stands the test of time, given that defining requirements for energy and nutrients is the fundamental bedrock of the scientific discipline of nutrition (Waterlow, 1979; Truswell, 1983; National Academy of Sciences, 1986).

Part of the reason for the apparent lack of clarity, or confusion, is that as our technical ability to make measurements has advanced and our understanding and awareness has developed, we have used different criteria to identify adequacy. Thus, at each stage there has been the tendency for 'the outcome of relevance' to be changed. As a consequence it has been necessary to change the way in which the relevant exposure is assessed, or the context within which the outcome of relevance has been derived. Initially the recommendations were prescriptive, with the clear objective of the need to achieve some minimum value

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of consumption which would sustain life (Truswell, 1983; Hollingsworth, 1984; Harper, 1987). As food availability increased, the concern has been less with the amount needed to achieve N balance, and more with qualitative criteria to achieve some less easily defined outcome related to good health. With the formulation of the most recent set of values in the UK, within the characterisation of the dietary reference values, every effort was made to move away from being prescriptive, with the explicit objective being to provide a reference without seeking to be judgemental (Department of Health, 1991). There are two other aspects of the dietary reference values of relevance to the present considerations. First, every attempt was made to ensure that the same acronym was not used to specify values which are conceptually different (the term recommended dietary allowance, or recommended daily amount, has been used rather indiscriminately to refer to different values; most confusingly it has been used to represent the mean for energy, but the mean +2 SD for protein; Food and Agriculture Organization/World Health Organization/United Nations University, 1985). Second, if the objective is simply to provide information for planning purposes at the level of the large group, the information needed is summative, with some sense of the extremes (mean requirement and the mean +2 SD), but with little concern for the factors which might contribute to the variability amongst individuals within the population. Increasingly, however, the reference values have found a use in the characterisation of diets for individuals, or to assess the adequacy of diets for special groups within the population. To meet this need it is necessary to have some information on the factors which underlie any variability in requirements amongst individuals. This process of clarifying the needs for reference values, and their appropriate use is ongoing. In relation to protein in the UK, it is possible to identify three major stages in the development of ideas over the recent past: the UK report of 1979 (Department of Health and Social Security, 1979); the work leading up to the Food and Agriculture Organization/World Health Organization/United Nations University (1985) report during 1980–5 (Torun *et al*. 1981; Rand *et al*. 1984), and the most recent UK report on dietary reference values, published in 1991 (Department of Health, 1991).

UK report (Department of Health and Social Security, 1979): recommended daily amounts

In the report of 1979, the recommendation identified that protein should contribute about 10 % of the energy in the diet (Department of Health and Social Security, 1979). The basis of the recommendation was the observation that this level was the level of intake which was seen in the population. As the population appeared to enjoy good health, this level of consumption must have been adequate.

It is worth recognising that even for the outcome of enjoying good health, there would be very wide differences in the protein requirement using this approach (infants less than 5 % based on breast milk, the elderly about 20 % for sedentary lifestyle, whereas adults might consume approximately 10–15 %). The reason for the variability is less related to the requirement for protein, than to the changing relationship between energy and protein requirements at different ages as the energy needs for growth and/or activity change (Jackson, 1995; Golden, 1997).

Food and Agriculture Organization/World Health Organization/United Nations University (1985) expert consultation: energy and protein requirements

In preparation for the international expert consultation on energy and protein requirements held in 1985, there was a considerable amount of background work to address a series of practical questions related to the way in which the recommended daily amounts were derived (Torun *et al*. 1981; Rand *et al*. 1984):

information had to be collected in relevant populations around the world;
different ages and genders had to be studied;
the relationship with energy intake and energy balance had to be considered;
data were required from short-term and long-term studies;
the outcome measures of importance were the achievement of N balance and weight maintenance (constant body composition) in adults, and positive balance in children.

The emphasis was on ‘protein quality’, i.e. the requirement for essential amino acids, with little specific consideration of non-essential N, and explicitly ignoring any possible relevance of the effects of colonic fermentation. There was no consideration of the needs for catch-up growth or weight gain, and the objective was to define a value which would allow for the maintenance of health in otherwise healthy individuals, on the assumption that the consumption of energy and all other nutrients was adequate. The policy objective was to provide information for planning global food requirements, and identifying the proportion of the population at risk of food insecurity.

UK report (Department of Health, 1991): dietary reference values

More recently, the objective of defining requirements and recommendations has shifted, and with the consideration of the dietary reference values in the UK, these important conceptual differences were stated explicitly. For this exercise, the objective went further than a consideration of the minimum pattern of consumption to ensure that the needs of the population to maintain weight and N balance were being met, or even a concern about minimal needs for a national food policy. Rather, the dietary reference value started to recognise that needs of the population have to be considered on a disaggregated basis, based on specific individual factors.

Wider, more recent considerations: a demand-led system

The work which has been carried out in order to define the needs of the population appear to have generated a wider range of confusion. This confusion is because as new knowledge has been forthcoming the older assumptions have not always stood up to rigorous scrutiny. As data accumulate, the older concepts have had to be modified. Much of the classic literature was based on methodologies, such as balance studies, which are technically difficult to conduct with reliability, and only provide relatively insensitive end points. The wider application of isotopic probes to trace the fate of defined species through the body has forced a reconsideration of basic assumptions. This reconsideration has inevitably generated debate, and it is only very recently that we have seen some agreement and clarity emerge from that debate. What is clear is that the intensity of internal exchange (protein turnover) is considerably greater than dietary intake, and therefore the amino acids derived from the proteins consumed can at best only characterise one aspect of the system (Waterlow, 1995).

As the amount and pattern of dietary proteins changes from one situation to another, the body appears to defend a preferred state through a process of metabolic adaptation in which essential functions are protected and internal homeostasis maintained (Waterlow, 1968). The preferred state may differ with gender, maturation, physiological state, lifestyle, environmental challenge and pathological condition, but at all times the achievement of an effectively adapted state sets a demand for a particular pattern and amount of the different amino acids. The achievement of each preferred state identifies the particular needs, demonstrating how the body functions, and showing that in effect it operates as a demand-led system. Thus, in order to be able to make a clear statement about requirements, the nature of the demand must be characterised for any given state (Scrimshaw *et al.* 1996). The importance of thinking about nutritional requirements, and operating according to this principle, has been developed in a increasingly refined and detailed way for energy. This approach to requirements, made explicit for energy in the Food and Agriculture Organization/World Health Organization/United Nations University (1985) report, assisted greatly in thinking through the issues involved. However, the same principle has not been applied as explicitly to the needs for amino acids and other nutrients until relatively recently. Defining the demand, and how best it might be satisfied, is the first big issue of importance.

What are the outcomes of relevance which need to be measured with reliability?

The second big issue is to be clear about the outcomes which need to be measured either to characterise the preferred state for the body, or to identify when this preferred state has not been achieved, or is in serious danger of not being achieved. At any time there are a range of multiple demands on the system, some of which are more important than others, leading to a hierarchy of demand (Jackson, 1986). It is only possible to know that the system has failed if we are able to determine the extent to which the function or activity which is lowest in the hierarchy has been protected. For example, in general, protecting linear growth during early childhood appears to be relatively lower on the hierarchy compared with dealing with intercurrent infection; but to what extent might the hierarchy be determined by the relative availability of specific micronutrients (Beard *et al.* 1984)? These issues are complex and difficult and await resolution, but the first step is to obtain some measure of what the demand might be under normal circumstances, and to see how this demand changes in different situations.

Current issues of policy relevance

Demand for individual amino acids

Young and colleagues at Massachusetts Institute of Technology, Cambridge, MA, USA have played a central role in developing approaches which better enable us to determine the demand for individual amino acids (Young & Bier, 1987; Young *et al.* 1989). Essentially, the approach has been to measure the rate at which indispensable amino acids are oxidised in the body, and therefore the rate of irreversible loss. The assumption has been that this value therefore provides a direct measure of the rate at which these amino acids have to be provided if function is to be maintained at the same level. There have been criticisms of the theoretical basis on which this work is based, and these concerns will have to be resolved with time (Millward & Rivers, 1988; Millward *et al.* 1989; Millward, 1998). Nevertheless, Young's work has led him to the conclusion that the demands for indispensable or essential amino acids are much greater than the level of consumption required to achieve N balance (Young *et al.* 1989). The implications of Young's proposals are profound in terms of the ability to satisfy the current food requirements for populations around the world, and almost unimaginable in terms of meeting the needs of the projected population increase over the next decades (Young & Pellett, 1990; Jackson, 1995; Young *et al.* 1998). Thus, if we are to accept Young's data we have to ask whether there are other interpretations or different ways of looking at the system (Waterlow, 1996; Millward, 1999*b*). There are three points which are worth making in this context.

First, the term 'essential' or 'indispensable' amino acids derives from the studies of Rose and colleagues (Rose, 1957). The interpretation offered by Rose (1957) was that for these amino acids the body was either not able to make the amino acid at all, or not able to make sufficient to satisfy its needs under the conditions of the test. Recent work has shown that the colonic microflora may play an important role in this respect, and early evidence indicates the possibility that amino acids formed by the colonic microflora may be available to the host in functionally-significant amounts (Jackson, 1995, 1998). If this possibility were confirmed, the implications would be considerable and fundamentally change our perceptions of protein requirements. Our work suggests that part of the adaptive process involves a process through which urea-N is salvaged for further metabolic interaction by the colonic microflora (Jackson, 2000).

Second, if the process through which urea-N is salvaged is of functional importance, then the factors which lead to effective salvage are of interest (Waterlow, 1999). It appears that an adequate intake of N is required to drive the salvage of urea-N, and that minimal protein requirements might relate directly to this function (Meakins & Jackson, 1996).

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Third, a review of the literature leads me to the conclusion that at the level of protein intake which is required to achieve N balance (current reference nutrient intake, or recommended daily amount, 0·75 g protein/kg body weight per d), the intake of essential amino acids is adequate to meet the needs of normal function. However, this level of intake may not necessarily be adequate to meet the needs for the formation of sufficient amounts of critical non-essential amino acids (Jackson, 1995). Demonstrating this fact is difficult, because the pathways through which amino acids are formed are dependent on other nutrients as cofactors and regulators; further, the amino acid may have a buffer pool which can be drawn on in the short term. There is some evidence that when the demand for glutamine is increased, the capacity to form glutamine may not be adequate to meet the demands (GK Grimble, unpublished results), and similarly for glycine (Jackson *et al*. 1996). Thus, for non-essential amino acids there is the need to determine the demand for those amino acids for a range of pathways, and also to determine the maximum capacity at which they might be formed in the body, and nutritional or lifestyle situations which might place a constraint on that capacity.

The practical implications of these observations are of very considerable significance for the public health and clinical practice and require more detailed exploration.

The susceptibility to infection and illness

On a regular basis the body is faced with threats from the environment which pose physical, chemical and biological challenges. The integrity of the system is maintained through a complex system of non-specific and specific mechanisms, all of which place a demand on the available amino acids. We are beginning to appreciate the nature of these demands and how cytokine-mediated influences can change the hierarchy of functions which need to be satisfied, and which in themselves require different patterns of amino acids (Jackson & Grimble, 1990). The ability to mount an inflammatory or immune response, to cope with potential free radical-induced damage, to repair and heal tissue, and to recover from illness involves a series of processes which may be enhanced or inhibited by the relative availability of specific amino acids. At the global and domestic level there is a very high burden of infection and inflammation which modifies the individual and group demand for N, amino acids and proteins. How are the requirements best satisfied for the range of compounds which need to be formed under these circumstances, and which require an 'unusual' pattern of amino acids?

Normal growth and development

Normal growth and development is manifest as the net deposition of lean tissue, and a progressive increase in metabolic capacity. The programming of fetal metabolic competence, and hence the individual susceptibility to infective and chronic disease, is dependent in part on the delivery of nutrients to the fetus, which is in turn set up by maternal body composition and metabolic behaviour. Amino acids appear to have a critical role in these processes, but the specific effects of particular patterns have yet to be determined (Jackson, 1999*b*).

Concluding comments

Over the last decade there has been a shift of emphasis in nutrition research away from studies in N metabolism. There has been the simple assumption that 'there is no dietary problem with protein'. It is clear that we can no longer maintain that illusion, but equally we cannot simply go back to the former way of considering work in this area. Over the next period genomics and proteomics will generate a wealth of information. However, if we are to make sense of this information we shall need to ensure that we have an appropriate conceptual framework within which to think through the issues. Defining protein requirements for the individual and group still remains one of the most important challenges for nutritional science. We now have a very clear series of questions which need to be addressed if we are to make sense of the intriguing data which have been generated over the last 15 years. We need to know the nature of the interaction within the body of N, amino acids and proteins with the quality and quantity of energy available, and micronutrient status during normal growth and development, with lifestyle changes and during illness and recovery.

Protein requirements: Recommended daily amounts: Dietary reference values: Amino acid requirements

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