The Central African
Journal of Medicine

Volume 11 OCTOBER, 1965 No. 10

The Protein-Calorie Relation in Nutrition

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The term "protein" defines a class of major nutrients, all containing nitrogen in organic combination, distributed universally in living matter and without which life as we know it is impossible.

Protein has as its main function the maintenance and repair of living tissue and the promotion of growth. Protein can also be used for the production of energy, but the amount thus used in a healthy organism where plenty of energy from carbohydrates and fats is available is small. The body's need for energy, however, takes precedence over all other requirements, and if the supply of calories for this purpose is restricted, such as occurs in malnutrition, starvation or in various disorders of metabolism, protein will be used to make up the deficiency.

During the latter years of the nineteenth century the foundations of modern work on protein metabolism were well and truly laid, but later the importance of protein metabolism was overshadowed by that of the vitamins which held the stage for the next 20 or 30 years. During the last 20 years, however, investigations on protein metabolism have again come to the fore, especially as regards work on amino-acids, the final degradation products of protein and the form in which protein is mainly absorbed from the alimentary tract into the bloodstream.

Recommended requirements of protein have varied greatly from time to time, from 120 g. per day in early German work to 40 g. per day proposed by Chittenden (1909). Present-day recommendations range from 65 to 75 g., but it is impossible to present a hard and fast figure, for there is a variety of conditions which affect protein requirements, such as growth, pregnancy, infection and other special demands of the individual; such factors as digestibility, amino-acid pattern of the protein, and circumstances such as composition of food mixtures or meals, with special reference to the proportion of energy-producing components and possibly the part played by adaptation (Mitchell, 1944), must also be taken into consideration.

In short, protein requirements are not static but dynamic, and this point cannot be too strongly emphasised.

In connection with the concept of varying protein requirements, the report of the expert committee on protein requirements of the Food and Agricultural Organisation of the United Nations (1957) is worth study.

The committee recognised a tendency to give unjustifiable precision to data on dietary requirements of protein and attempted to counteract this tendency by making its recommendations elastic and by insisting on the need for further research. The report also indicates the direction from which the problem of protein requirements is being answered. Two main developments were emphasised. (1) The expression of human requirements in terms of an ideal reference protein of high nutritive value with 100 per cent. absorption; and (2) the adoption of a provisional pattern of the essential amino-acids listed by Rose *et al.* (1955) which cannot be synthesised by the body, and must therefore be supplied in dietary protein, and from which the nutritive value of any diet can be calculated from its amino-acid content where known. These figures are now available for a large variety of foodstuffs.

It has long been known that there is a close connection between protein metabolism and the caloric value of the diet, and protein supply must now be considered in connection with energy requirements.

When food is supplied in sufficient quantities to cover the consumers' energy requirements, the protein value of the food is determined by two factors: (1) the concentration of protein present; and (2) the quality of such protein.

Factor (1), concentration is obtained from determination of the nitrogen content (N) of the foodstuff. The result is converted to crude protein value by multiplying by 6.25 as the average nitrogen content of protein is 16 per cent.

The expression N x 6.25 appears in terms of weight, but can easily be expressed in terms of energy value or calories for 1 g. protein yields by oxidation 4 cals. We have, therefore, N x 6.25 x 4 cals. derived from protein, or protein cals., and these can be expressed as a percentage of the total calories available, i.e.:

$$\text{P. Cals. \%} = \frac{\text{Total calories that could be obtained from P}}{\text{Total metabolisable calories}} \times 100$$

Under normal conditions and with a good mixed diet the amount of calories derived thus from protein is small, usually not more than 10 to 12 per cent. of the total calories.

Factor (2), quality, is measured by direct or indirect determination of the proportion of dietary protein nitrogen retained by the consumer, taking into account the biological value and digestibility of the protein.

The proportion $\frac{\text{Nitrogen retained}}{\text{Nitrogen intake}}$ is termed the Net Protein Utilisation, or NPU, which gives the proportion retained in terms of a conventional reference protein with 100 per cent. retention as proposed by FAO. NPU can also be obtained in terms of digestibility and biological value, for digestibility is defined as $\frac{\text{N absorbed}}{\text{N intake}}$ and biological value as $\frac{\text{N retained}}{\text{N absorbed}}$; thus

$$\frac{\text{N absorbed}}{\text{N intake}} \times \frac{\text{N retained}}{\text{N absorbed}} = \frac{\text{N retained}}{\text{N intake}}$$

or NPU as defined above.

NPU can be determined directly or indirectly. A direct determination is made by estimation of N intake and retention in young rats fed on the diet under investigation over a fixed period. The determination can be completed in as little as 10 days (Miller and Bender, 1955).

Indirect determination is made by recourse to the provisional pattern of essential amino-acids referred to above. This method requires the composition of the foodstuff under investigation to be determined by means of the tables issued by FAO and the amino-acid "score" computed. If the quantities of essential amino-acids calculated as g/g N are determined and found to be present in amounts at least as great as those recommended by FAO in their adopted "provisional" pattern (FAO, 1957), the score will be 100 per cent. and the NPU 100 per cent., but any of these amino-acids present in less than the recommended quantity will lower the score proportionately.

From an inspection of the FAO tables it can easily be found which of the amino-acids is present in the smallest quantity, and that which has the lowest "score" will have the most limiting effect on quality, i.e., on NPU. In calculating the "score" for a meal as opposed to a single foodstuff it must be remembered that the total amino-acid content of the whole meal is to be used. Theoretically each amino-acid should be scored to ascertain which is the most limiting. In practice, however, it is sufficient to search for three only in particular: (1) the sulphur containing amino-acids, cystine and methionine; and (2) where the protein source is mainly cereal, lysine. Having ascertained which of these amino-acids is present in least amount, the calculation can easily be made, using information from food composition tables to find the total amount of the limiting amino-acid present as a proportion of the total nitrogen present. The "score" is determined by expressing the former as a percentage of the figure recommended by FAO.

Example: Using the amount of sulphur containing amino-acids (S.A.A.) for which the FAO factor is 0.27 g/g N as the limiting amount, suppose the total N present in the sample is 2 g. and the total amount of S.A.A. present is 0.4 g., then the score will be $\frac{0.4 \times 100}{0.27 \times 2} = 74\%$.

This calculated chemical score is quite close to the figures obtained for NPU by bioassay of the food in question on rats as given above and has also been calculated for some human diets with quite good agreement (Miller and Payne, 1961b, 1961c). The calculated chemical "score" equals the NPU only when the level of protein intake is low, for as the protein concentration increases, so does the NPU fall.

The product NPU x protein concentration, i.e., NPU x N x 6.25, is a product of quantity x quality expressed as a percentage of an ideal reference protein and is termed the Net Dietary Protein Value (NDPV).

The expression of NDPV can be given as a percentage of dry weight of the foodstuff, but this does not always give a true picture of protein availability, for as Miller and Payne (1961a) have shown, diets containing the same utilisable protein at *equal energy content* have the same dietary value despite possible wide differences in composition. It is therefore useful to express NDPV also in terms of energy value, i.e., protein calories as defined above. This is given by the expression NPU x N x 6.25 x 4 and is termed the Net Dietary Protein Calories % (NDpCals%).

The requirements for NDpCals% of various human categories have been set out by Platt *et al.* (1961). Infants require 8-9 NDpCals%, which is the value of breast milk, after which the curve of NDpCals% requirements plotted against age (Platt *et al.*, 1961) sinks to 6-7 for small children, rises to 7-9 for adolescents and falls again to 4-5 for adults. Pregnant and lactating women require 8-9.

A nomogram has been constructed by Miller and Payne (1961b) which can be used for calculating NDpCals% of various diets and foodstuffs.

The differing needs of consumers in both physiological and pathological circumstances have long been recognised, but have not yet been precisely stated in simple terms.

Protein malnutrition in man is frequently associated with low intakes of foods which may have an adequate protein value if consumed in unrestricted amounts; but because energy requirements are always satisfied in preference to protein requirements where diets of a low energy content are concerned, it is found that an increasing amount of protein is burnt for energy purposes, and consequently the efficiency of utilisation of protein, NPU, decreases.

Thus when the food intake of rats was reduced from 8 to 6 g. per day there was no change in biological value, but a decrease from 99 to 69 when the food intake was further reduced to 4 g. per day (Forbes and Yohe, 1955). One might, therefore, expect for any given diet a range of food intakes over which NDpCals% is constant and below which it tends to fall with the reduction in calorie intake.

Under conditions of calorie restriction the protein value of a diet depends upon the energy available for protein anabolism *after* other energy requirements have been satisfied rather than on the concentration and nature of the protein it contains. This expectation has been fulfilled experimentally (Miller and Payne, 1961b) and is a finding with important implications in human nutrition. Indeed, it may be asserted that *pure* protein deficiency is very rare in man, there being nearly always a change in the calorie intake as well. Protein-calorie deficiency can be seen on a large scale in many parts of the world in all degrees of severity, mainly, as one would expect, amongst young children whose protein and calorie needs are relatively enormous. The two extreme forms of protein-calorie deficiency, marasmus and kwashiorkor, are well-known clinical entities. Platt, Heard and Stewart (1958) have shown that piglets fed on a low protein diet of NDpCals%=3.4 develop a syndrome resembling marasmus in children, and if this diet is supplemented with additional carbohydrate to produce a final NDpCals% of 2.5 a form of protein malnutrition resembling kwashiorkor is precipitated. Piglets on both these protein-calorie deficient diets exhibited a variety of abnormalities, biochemical, physiological and histological, embracing many systems.

Well-marked changes occur in the alimentary tract, and although most of these changes cannot be demonstrated in the intact living animal, one change, that occurring in the superficial buccal epithelium and which is easily reversible on changing from a deficient to an adequate diet, can easily be demonstrated in animals and humans (Squires, 1963, 1964).

Congenital Malnutrition

Many of the changes found in experimental animals subjected to protein-calorie deficiency can be regarded as evidence of delayed maturity; further, in general the most severe disturbances are in animals in which protein-calorie deficiency has been established at an early age. The possibility of inducing changes in the foetus by producing malnutrition in the mother has, therefore, been considered (Platt, 1962).

Young growing bitches were given a diet low in protein (NDpCals=6.8%), but otherwise adequate. Cinematograph records showed that the offspring were retarded and development and exhibited a peculiar disorder of movement with extremely clumsy gait, tremor of the head and unusual postural reactions. These symptoms tended to disappear as the animals grew older, but the central nervous system showed lesions similar to but more pronounced than the changes reported in piglets suffering from protein-calorie deficiency. Many of the pathological changes already listed for the normally born animal subjected to protein-calorie deficiency have been found in pups born of malnourished mothers, and the condition of the pups might well, therefore, be regarded as a congenital malnutrition syndrome.

Protein-Calorie Deficiency and Pathogenesis

There has been and still is a widespread tendency to confine the effect of malnutrition on pathogenesis to those syndromes generally classed as being due to dietary deficiencies. Protein-calorie deficiency can be expected to develop in any animal attacked by disease in which there is increased need for protein which is not satisfied for various reasons, including the most important one of loss of appetite.

Many years ago Macallum (1910) drew attention to the loss of protein which occurs during the fever accompanying bacterial infection. He quoted observations of losses of 3.2 kg. of muscle tissue in 12 days and 2.5 kg. in eight days, and noted that this loss was greater during the period of defervescence. More recently it has been found (Grossman *et al.*, 1945) that the protein losses in meningitis were large and prolonged—up to 180 g. This latter loss, which is equivalent to 4.5 kg. of muscle, was accompanied by a loss of 7.5 kg. in body weight, and Browne *et al.* (1954) have found that similar losses may occur in convalescence.

The mechanism of this obligatory loss of protein, which has been termed the toxic destruction of protein, is not well understood, although Payling Wright (1958) suggests that metabolic adjustment due to the diversion of certain amino-acids to meet increased defence needs may be a major factor. It may be in part related to the so-called metabolic response to injury such as occurs in fractures, burns and surgical operations. If the patient ingests protein exceeding that needed to maintain nitrogenous equilibrium before illness, he will replenish the depleted stock of protein, provided that the total calorie intake is sufficient. Such need for extra protein may be very great, e.g., Payling Wright (1958) has pointed out that a leucocytosis of 30,000 wbc per c.mm., a very ordinary level in suppurative pyococcal infections, entails the provision of between 10 and 20 g. protein daily.

Parasitic Infection

There is also an inter-relationship between protein-calorie availability and parasitic infection, for it has been shown by Platt *et al.* (1961), in rats infected with the rat malarial parasite *P. berghei*, that the protein value of the diet to the infected rat as measured by nitrogen retention was only about half that for the uninfected control animal. About half of this reduction was due to impairment of appetite, the remainder being due to the failure of the animal to use nitrogen for normal physiological purposes. Like results have been obtained for helminthic infestations.

The above description of the protein-calorie relationship attempts to stress the importance of this concept in various aspects of applied nutrition, and in conclusion some account of suggestions for detection of this deficiency will be given.

Of recent years much attention has been paid to health problems of under-developed countries, and amongst such people protein-calorie deficiency is a pressing problem (Jelliffe, 1959).

The magnitude and specific nature of the problem need to be defined as a preliminary measure to action directed towards control. The assessment of protein-calorie deficiency, especially in the early stages, is therefore necessary, and this requirement brings us to consideration of early signs of such deficiency. The report of the FAO expert committee on nutrition (1958) suggested that "there is need for simple objective "nutrition indicators" which can be used by public health workers with a limited knowledge of nutrition, but there are no universally recognised specific, easily performed tests for this deficiency.

Bengoa *et al.* (1959) have suggested various potential indicators for broad assessment from the following sources: (1) vital statistics; (2) anthropological measurements; (3) clinical signs; (4) figures of food consumption; and (5) laboratory tests.

(1) *Vital Statistics.*—Any figures obtained from vital statistics depend entirely upon the proper functioning of the local administrative machine for their success. When no official machinery exists an approximate figure may often be obtained by persistent inquiry at, e.g., mother and child welfare centres.

Since children under one year of age are afforded some protection by breast feeding, and since the school age child, about five years, can make its needs for food known and can actively compete for food, the chief impact of protein-calorie deficiency tends to fall upon the 1-4 year age group; it would therefore appear that the mortality rate in this group might be a good indicator of the degree of severity of protein-calorie problems in that region.

Bengoa and his colleagues (1959) are of the opinion that where mortality in the 1-4 year age group is more than 10 per 1,000, it could probably be related to a serious protein-calorie deficiency, although they admit that other factors might contribute to the high mortality.

Wills and Waterlow (1958) have suggested that the ratio

$$\frac{\text{death rate of age group 1-4 years}}{\text{death rate of infants under 1 year}}$$

might serve as an index and give examples.

(2) *Anthropometric Measurements.*—A large variety of these measurements has been suggested from time to time, but in practice the only ones to be considered from the point of view of simplicity are weights and limb girth measurements. It is true that height measurements are also simple, but the inherent error of height measurements is greater than that of weights and should be used only in longitudinal surveys.

Birth Weights: It is generally agreed that the nutritional status of the mother has some influence on the weight of the foetus along with other factors such as racial and genetic influences, age of the mother, sex, plurality of birth and the effect of certain diseases.

Platt (1954) has suggested that a record of birth weights may prove a useful indicator of this deficiency, and Bengoa *et al.* (1959) suggest that the best way of using the birth weight as an indicator would probably be to give the percentage of birth weights below a conventional arbitrary figure, e.g., 2.5 kg. (which figure corresponds with the prematurity index), for the average of total birth weights in a given population will not show the variations which exist in regions with different levels.

Childhood Weights: Gomez *et al.* (1956) have advocated for some years that a classification of malnutrition in early childhood into three degrees on the basis of weight deviation from standard weight for the groups should be adopted thus:

First degree of protein-calorie malnutrition; 75-90 per cent. average weight.

Second degree of protein-calorie malnutrition; 60-75 per cent. average weight.

Third degree of protein-calorie malnutrition; under 60 per cent. average weight.

This method is said to have been used with some success in Central America even when children's ages have had to be guessed, based on the age as stated by the mother checked against the date of some well-known local event. It is of course necessary to obtain the local average weights from a previous study, although standards obtained from elsewhere may be used provided that such standards are clearly defined.

Muscle and Fat Measurements: According to Bengoa *et al.* (1959), the upper arm circumference has been tentatively suggested This suggestion is based on the fact that in all forms of protein-calorie malnutrition in pre-school children, muscle wasting appears as a prominent feature, and the mid-arm circumference at the level of the belly of the biceps can be simply measured. Average values for healthy children of the population must of course be known.

(3) *Clinical Signs.*—A number of clinical signs of protein-calorie deficiency has been described, very few of which are specific. One that can be easily elicited is the "pluckability" of hair. The sign is obtained thus: a group of 20 to 30 hairs from the anterior half of the scalp is taken between the thumb and the index finger and pulled firmly and steadily. In a child suffering from protein-calorie deficiency 10 or more hairs can be plucked easily and without pain. Bengoa *et al.* (1959) state that a significant statistical relationship has been found between the occurrence of this sign and weight.

(4) *Figures of Food Consumption.*—Such figures have been recommended, but may be of little value in this connection, for the average availability of food is not necessarily a measure of nutritional intake, nor can the figures be applied by ordinary public health employees.

(5) *Laboratory Tests.*—In spite of the tremendous advances made in this field, there are very few simple tests available for field surveys. Platt and Heard (1958) have suggested the determination of urea nitrogen and ammonia nitrogen as a proportion of the total urinary nitrogen as a simple method of assessing nutritional status with respect to protein. This test should be very simple, as a single morning specimen of urine would provide the necessary information.

The estimation of haemoglobin may have its use as such an indicator, especially in conjunction with other indicators.

Finally, it must be emphasised that the use of these indicators should not replace the traditional anthropometric survey, clinical survey or institution of laboratory tests in a given population; but if the answers given by these indicators only go so far as to rouse suspicion of protein-calorie deficiency, then the use of indicators by relatively unskilled personnel will be justified.

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