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Nutrient interrelationships as they affect the formulation of balanced diets

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In 1963, and for that matter during the years immediately ahead of us, there is not a more important topic in nutrition than the effect of nutrient interrelationships

upon the requirements of homothermic animals for specific components of the diet. Research-wise, we are in the midst of an era in which nutrient interrelationships are receiving an ever-increasing amount of attention, and the nutritionist is recognizing the extreme complexity of his task of determining truly meaningful requirement figures for the various nutrients that apply to the different animal species.

For those who are concerned primarily with the nutrition of domestic animals, the problem of recognizing nutrient interrelationships in diet formulation is alleviated to some degree by the use of electronic data-processing equipment. However, it must be kept in mind that the usefulness of the computer is restricted to the limits of the knowledge of its operators. The researcher must first determine the biological significance of specific nutrient minimum, maximum or absolute levels before the computer can be expected to carry out an effective service. The determination of such values is becoming increasingly difficult as each additional interrelationship between nutrients becomes known.

Those who are concerned primarily with human nutrition are faced with additional problems. These are, of course, centred around the habits and prejudices of man with regard to the consumption of specific foods. In the field of human nutrition, a diet that recognizes all known nutrient interrelationships might be formulated, but there would be no assurance that it would prove acceptable to the group of individuals for which it was intended.

It would be an extremely misguided hope that all nutrient interrelationships that affect the formulation of balanced rations or diets might be covered in a single paper on the subject. However, an attempt will be made to select certain interrelationships which currently are of particular interest, with the hope of emphasizing the type of problems encountered in formulation as a consequence of interdependence between nutrients.

Though interest in the interrelationships that exist between many of the nutrients represents a modern trend in nutrition, the fact that certain interrelationships have been recognized for many years cannot be ignored. Among the better known of these might be included the close association between (1) calcium, phosphorus and vitamin D, (2) nicotinamide and tryptophan, and (3) iron and copper. Because so much has been written about these over the years, they will not be covered in this paper. Nor will any attempt be made to document all references to specify nutrient interrelationships, as this will have been done in most instances by earlier participants in this Symposium.

The high-fat diet or ration

There are two classical examples of the consumption of high-fat diets by groups of 'animals'. It has been well publicized that the average North American consumes an assortment of foods that provides over 40% of its calories in the form of fat. It is not my intention to enter the controversy of the relation of such a diet to the development of atherosclerosis and coronary heart disease. At this time, it would seem more appropriate to consider the consequences of the consumption of fat at levels of this magnitude upon the requirements for other dietary nutrients.

In the early 1950s, poultry nutritionists began to increase the energy concentration of broiler diets by the direct addition of edible fats. As a result, many modern broiler diets contain 5% of added fat. What are the practical consequences of such additions?

In the first place, high-fat diets are thought to have a thiamine-sparing action. This idea originated with the findings of Evans & Lepkovsky (1929) that high levels of fat delay the onset of signs of a deficiency of vitamin B₁. This delay has since been attributed to the fact that either (a) less thiamine is used in the metabolism of fat than of carbohydrate, or (b) the rate of thiamine utilization is unchanged regardless of diet composition, but fat in some way exerts a protective effect against the onset of deficiency signs. In most instances, increased excretion and decreased tissue levels of thiamine have been found to result from diets low in fat and high in carbohydrate. However, regardless of the physiological mechanism involved, the thiamine-sparing action of high-fat diets is of minor practical significance in most human dietaries and of no real importance in poultry diets in which adequate levels of thiamine are achieved through natural ingredients.

Of more importance is the effect of high-fat diets on the requirements for vitamin E. Included among the better-known signs of vitamin E deficiency are muscular dystrophy in different species, foetal resorption in rodents, testicular atrophy in rats and chicks, encephalomalacia and exudative diathesis in chicks, dental depigmentation in rats and susceptibility of red blood cells to oxidation haemolysis in several species, including man. All these signs develop more quickly when a source of unsaturated fat is included in the diet, and many will not develop in the absence of dietary fat (see review by Murray, 1963).

In view of certain recommendations that diets containing high levels of polyunsaturated fats be consumed by man in order to lower blood cholesterol levels and because of the susceptibility of the chick to avitaminosis E, the interrelationship between this vitamin and the level and character of dietary fat becomes of concern in formulation of the diets or rations. The use of a vitamin E : polyunsaturated fat ratio has been suggested, and this method could be meaningful in assessing the adequacy of diets or rations with respect to vitamin E since it expresses directly the influence of polyunsaturated fats on the requirement for vitamin E.

Murray (1963) has pointed out the lack of agreement on the role of dietary fat in the absorption of vitamin A. There is evidence that some fat is essential for the efficient utilization of vitamin A and carotene, but equal support exists for the view that dietary fat is unnecessary for this purpose. Murray's personal conclusion is that a fat that is poorly absorbed or one that would lead to the rapid destruction of vitamin A must have an adverse effect on utilization, but that there are not any more subtle effects of dietary fat on vitamin A utilization. Therefore, it would appear that where high-fat diets or rations are used recognition must be taken of the absorbability of the fat and the presence of tocopherols, with or without other antioxidants, in the carrier in relation to the recommended levels of vitamin A.

Super-supplementation

There are well-known circumstances in which calcium is being consumed in what would appear to be excessive amounts. During pregnancy and lactation, it is not uncommon in certain areas of the world to find the human female consuming daily a supplementary source of Ca, thus providing an intake considerably in excess of her requirements. In poultry nutrition, levels of 5% Ca have been recommended for layer diets, even though optimum egg-shell formation can be accomplished with less than 4%. Only for pigs has the recommended level of dietary Ca shown any apparent downward trend.

Ca is indeed an indispensable nutrient, and for years a primary responsibility of the nutritionist was to ensure that it was present in all diets in liberal amounts. However, some recent findings have tended to point to Ca as an enigma in diet formulation. It may be worth while considering very briefly some of the considerations that may force us to conclude that the maximum level of Ca is not necessarily the optimum level under all conditions. First, the interference by Ca with the utilization of certain trace elements must be considered. The story of pig parakeratosis provides an excellent example of the action of Ca in this sense. The discovery that this condition could be prevented or cured by the addition of Zn to the diet was most important, but more pertinent to this discussion was the finding that high levels of dietary Ca aggravated the condition. Therefore, Ca apparently interferes in some way with the utilization of Zn, and a parallel has been drawn between this effect and the aggravation by Ca of manganese deficiency signs in poultry.

More recently, it has been shown that Ca has an inhibiting effect upon the absorption of certain antibiotics. This problem is of special significance in the poultry industry in which the diets used may be particularly rich in Ca and antibiotics are so routinely used in the control or eradication of various diseases. This has led to research designed to raise antibiotic levels in the blood and has involved such methods as a drastic reduction in dietary Ca over a short period of time, or the use of chemicals that will tie up the Ca and thus prevent it from exerting its inhibitory effect on antibiotic absorption.

In a relatively recent experiment at Macdonald College (Costain & Lloyd, 1962), it was found that a hog grower ration containing Ca at a level 35% below NRC requirements ((USA) National Research Council, 1959) resulted in a significant improvement in food conversion efficiency. A report from Florida by Combs & Wallace (1962) typifies the findings of many with regard to Ca. In three experiments with early-weaned pigs, in which Ca levels of 0.40 and 0.88% were compared, the higher level significantly depressed growth rate. Similar differences in growth rate were obtained with diets containing either 0.52 or 0.70% Ca. When the Ca content was increased by increments of 0.10 from 0.40 to 0.80%, daily gains tended to decrease linearly with increasing Ca level. On the other hand, it has been shown that levels of 0.8–1.0% Ca are necessary for normal bone formation in the young pig (Miller, Ullrey, Zutaut, Baltzer, Schmidt, Hoefler & Luecke, 1962).

The published requirements for dietary Ca have been determined, for the greater

part, on the basis of amounts required for normal bone growth and development. However, because of the role of Ca as an antagonist in the utilization of certain micro-nutrients, is it possible that optimum levels of Ca for bone development are not necessarily optimum for the growth and development of other tissues? If this were true, the inclusion of Ca at levels below current recommendations in diets for animals destined to be marketed at a relatively early age (i.e. hogs and steers) might have some beneficial effects. The objective might be to obtain greater and more efficient gains at the expense of maximum bone strength, without of course interfering with the mobility of such animals during their restricted life span.

There are certain situations in which iron is administered in fairly large amounts as a precautionary measure against anaemia. As with Ca, it is so mainly with the pregnant woman. One other instance pertains to the claims that are sometimes made for allowing young pigs free access to Fe and for the use of high dietary levels as growth stimulants. The indiscriminate administration of large quantities of Fe may present problems.

The effect of the ingestion of excessive amounts of Fe upon phosphorus utilization has been known for some time, but little research has been done on this inter-relationship during recent years. Waltner (1927) demonstrated that excess Fe would cause P deficiency signs in rats. Similar findings were subsequently recorded by Cox, Dodds, Wigman & Murphy (1931) in guinea-pigs, by Deobald & Elvehjem (1935) in chicks, and by Brock (1937) in man. The principal signs observed were lowered levels of serum inorganic P and femur ash, and mostly the effect could be overcome by increasing the P content of the diet. In view of these findings it might be considered advisable to provide the pregnant woman and the young pig with supplementary P whenever the dietary level of Fe is high. For the pregnant woman, it might be that under certain conditions supplementary P is of equal or greater importance than the provision of high levels of total dietary Ca.

During the past 5 years, the North American incidence of vitamin A deficiency in steers under feedlot (i.e. non-grazing) conditions has increased markedly. The deficiencies have ranged from mild to severe, and have been observed in beef cattle consuming diets previously considered, from their carotene content, to contain adequate levels of vitamin A. It is not necessary here to discuss the various suggestions that have been made to explain this occurrence, but the result has been the supplementation of beef-cattle diets with vitamin A ranging from 10 000 to 40 000 i.u./head daily. According to current feeding standards, a 1000 lb steer requires about 7000 i.u. of the vitamin daily.

Though there is evidence that the ingestion by steers of 2 560 000 i.u. vitamin A daily for a period of 168 days will not produce toxicity signs, the question remains as to the consequence of the continued ingestion of amounts of this vitamin that may be six times the recommended intake. It has been claimed that carotene can interfere with the antirachitic action of vitamin D, particularly when the levels of the latter are low. The evidence is not conclusive but, because of the chemical relationship between carotene and vitamin A, the possible deleterious effect of high levels of the latter on vitamin D metabolism cannot be completely discounted.

The importance of protein adequacy

What is really meant by protein adequacy? Certainly the answer given to this question in 1963 would be quite different from that given 30 years ago, and it is not inconceivable that the answer provided in 1993 again will be dissimilar to our current concept of adequacy. This applies not so much to quantity of protein in the diet or ration—rather the variance lies in the quality of the protein.

When we speak of protein quality today, we must consider the many variables that may exert direct or indirect influences. For example, in addition to amino acid balance, we must be aware of the interrelationships between essential and non-essential amino acids, the relative biological values of D- and L-amino acids, and the effect of level of protein on the requirements for specific essential amino acids. In addition, protein-vitamin and protein-mineral interrelationships must be recognized. As factors that may influence the required dietary level of protein, we must consider the possible protein-sparing action of non-protein nitrogenous compounds in the diet as well as that of certain carbohydrates and fats.

Interest in the protein status of the human and the domestic animal populations in developing countries is great at the moment. Thus it may be of interest to consider the complications arising from the consumption of diets or rations of inadequate protein content—i.e. complications primarily that are the consequence of nutrient interrelationships. Obviously, it would be impossible to cover here each of the interrelationships listed above. Perhaps a limited number of examples will suffice to indicate the complexity of the problem.

As one example, it has been shown clearly, with both the human and other animal species, that the consumption of low-protein diets will result in poor retention and utilization of riboflavine. Under such conditions, the level of riboflavine in the organs is low and its excretion in the urine is high, increasing with higher intakes of the vitamin. It has been suggested that the cause of suboptimum riboflavine retention during periods of protein inadequacy is the high lability of the flavoproteins. That is, during negative nitrogen balance the labile proteins are lost first, and when they are reduced dietary riboflavine cannot be utilized because the proteins with which it would normally combine are not available.

From these observations, Murray (1963) has pointed out that during times of negative nitrogen balance, the requirement for riboflavine, as measured by urinary excretion, appears to fall. This in fact is not correct since, under these conditions, only large intakes of the vitamin will prevent the appearance of signs of riboflavine deficiency, and then only for a short period. This example indicates the danger of underestimating the requirement for riboflavine in any group of individuals commonly exhibiting a negative nitrogen balance.

A second example would be the consequence of the consumption of inadequate protein diets or rations upon the utilization of vitamin A. In this instance, the experimental results are not as conclusive as with riboflavine. For instance, some workers have shown that rats fed on diets low in total protein will store less vitamin A than those whose intake of protein is normal, and that poor-quality protein will

have the same effect. In contrast, others have shown no effect of protein intake upon vitamin A absorption or storage. Though it cannot be said definitely at this time that diets inadequate in protein will interfere with the absorption and storage of vitamin A, Murray (1963) suggests that it is likely that the utilization of carotene is impaired by protein deprivation. In addition, he points out that there is little doubt that in most animal species severely depleted of protein the utilization of liver reserves of vitamin A is retarded.

From these observations it is clear that protein deficiency signs of populations existing on diets low in protein content or of poor protein quality may be confounded with signs of riboflavine deficiency and of avitaminosis A. It should be kept in mind as well that, under such conditions, the requirements for these two vitamins may be considerably in excess of the usual recommended levels.

Energy as a basis for establishing nutrient requirements

In discussing the protein adequacy of diets or rations, reference to the relationship between protein content and availability of energy was intentionally omitted. It seemed more opportune to consider this extremely important interrelationship at this particular stage.

It has become an accepted fact that monogastric animals will consume sufficient amounts of food to meet their requirements for energy. This fact became of extreme practical importance with the advent of high-energy broiler diets during the early 1950s. With the reduced consumption of feeds containing higher levels of available energy, it became obvious that the protein concentration of such diets had to be increased to ensure an adequate intake of protein. Thus, it is now an accepted fact that protein requirement can be defined accurately only in relation to energy concentration of the diet, as opposed to the previous system which was in terms of the percentage of protein per unit weight of diet dry matter. Whereas this line of thought has excluded to date the ruminant species of animal, recent evidence from our laboratory (Donefer, Lloyd & Crampton, 1963) suggests that, at least under certain conditions, such animals may follow a similar pattern with regard to intake of high-energy rations.

Recently, Crampton (1963) compared the published maintenance energy requirements of adults of different species of animal with their needs for digestible protein. The species compared included man, ox, horse, pig, sheep and rat, with a weight range from 0.55 to 454 kg. In all of them the ratio in g of digestible protein required daily per 1000 digestible kcal of dietary energy was close to 19, indicating that the optimum protein : calorie ratio is independent of species or size. He also stated that during the last trimester of pregnancy, the protein : calorie ratio might be increased to 22, but that during lactation and increased physical activity (work) the increased intake of total food would preclude any necessity of changing the maintenance protein : calorie ratio. With regard to growing individuals, including man, Crampton has suggested three 'growing' diets, with changes in g digestible protein/1000 digestible kcal from 28 to 23 to 21 to the adult 19 g, these changes being introduced when 22, 35, 72 and 100% respectively of adult metabolic weight has been attained.

Since protein requirements can be associated so closely with energy intake, what opportunities are there for expressing the requirements for other nutrients with energy as a base-line? It is quite obvious that most of the B-vitamin complex will fall into line, but what of the minerals and fat-soluble vitamins? Crampton (1963) claims that the latter problem may be circumvented by equating the nutrient requirements to dietary energy levels rather than directly to the individual. This approach requires first a tabulation from existing standards of the amount of each of the nutrients required per 1000 kcal diet and then a determination of the energy requirement of the particular individual or group. As an illustration, a tabulation of some of the nutrients required per 1000 kcal was presented for man and is reproduced as Table 1. In order to convert these figures to daily nutrient needs, we must have values for the necessary daily energy intake. These values can be read from a chart showing the

Table 1. *Daily nutrient requirements of man per 1000 dietary kcal (from Crampton, 1963)*

Nutrient	Adults, all categories	Juveniles		
		To 20 lb	20-40 lb	Over 40 lb
Protein:				
BV 100 (g)				
BV 75 (g)	13.5	28.0	25.0	20.0
BV 50 (g)	21.2			
Calcium (g)	0.22	0.7	0.5	0.48
Phosphorus (g)	0.22	0.7	0.5	0.48
Iron (mg)	2.6	5.0	3.5	4.8
Thiamine (mg)	0.2	0.40	0.28	0.32
Riboflavine (mg)	0.3	0.60	0.43	0.52
Nicotinic acid (mg)	1.0	4.0	2.8	3.2
Ascorbic acid (mg)	13.0	20.0	14.0	12.0
Vitamin A (i.u.)	1900.0	1000.0	700.0	1400.0

BV, biological value.

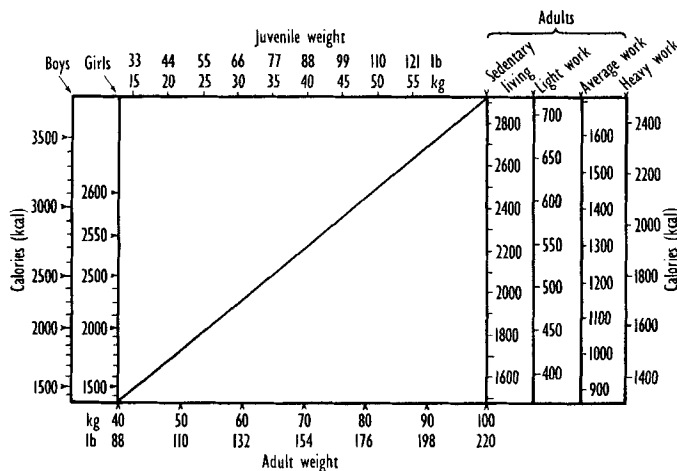


Fig. 1. Daily calorie requirement related to body-weight for boys and girls, and for adults living a sedentary life, and daily increments necessary for adults doing light, average or heavy work.

regression of calories on body size, the degree of activity being taken into account for the adult individual. Crampton (1963) presented a chart designed to facilitate 'reading off' such values, and it is reproduced here as Fig. 1. From this chart, the daily energy requirements of juveniles and of adults living a sedentary life may be obtained directly. For adults at work, a second reading from the appropriate activity scale must be taken and added to the sedentary value to provide an estimation of the total daily requirement.

Thus, though the requirements for certain nutrients may not be related, in the strictest biological sense, to energy intake, there is a definite establishable relationship to the latter through body size. Crampton summarizes by stating that, 'It seems that there is valid evidence to justify the conclusion that energy intake, directly or indirectly, determines for most nutrients the intake that is compatible with maximum efficiency of the diet as a whole, in the maintenance and productive performance of the animal body'.

Though there may be isolated exceptions to this argument, as with specialized diets determined by pathological conditions and for extra supplementation with Fe, Ca and P during the latter stages of pregnancy, the overall theory of using energy as a base-line in diet or ration formulation appears to be sound.

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