

TRABAJO DE REVISION

Amino acid fortification

HANS D. CREMER¹ AND JEAN MAURON²

SUMMARY

After a short introduction on the need to increase and improve the protein supply for large parts of the world's population the problem of amino acid supplementation has been dealt with from different angles. Examples for imbalanced food and supplements have been given and the possibility of deleterious effects has been described. Nutritional, medical, and economical aspects have been discussed.

Amino acid fortification of a staple food or other foods appears to have become feasible from the economic point of view. More information is required on the effectiveness and health benefits of its practicable application under conditions of every day living in the developing countries of the world.

INTRODUCTION

There is no doubt that for a large part of the world's population food supply is inadequate in either quantity or quality. The group mostly hazarded by an insufficient diet are children, especially in the preschool age. Stunted growth caused by protein calorie malnutrition occurs in many, often in nearly all preschool children in less developed countries during weaning and in the post weaning period. Children with insufficient supply of food protein may develop chronic malnutrition which even if it remains in a subclinical phase makes the children more susceptible to morbidity and mortality from various infectious diseases. Increasing and improving the protein supply is therefore one of the most important nutritional problems for developing countries.

¹ Institute of Nutrition, Justus Liebig University, Giessen (Germany).

² Research Laboratory of Nestlé's Products, Vevey (Switzerland).

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The quality of a protein depends on its amino acid composition. The low biological value of most plant proteins is caused by the fact that one or more of the essential amino acids do not occur in sufficient quantity in that particular protein. From the purely scientific point of view there could not be any doubt that addition of the missing amino acid(s) would improve the biological value of plant proteins. But from the practical point of view there is some controversial discussion whether supplementation by one or a few amino acids could be a way, better, one of the ways and means to equilibrate the amino acid balance and so to solve the protein problem or at least to contribute to its solution.

Implicit in the concept of the equilibration of the amino acid balance was the assumption that, although the efficiency of utilisation of an unbalanced protein is low, the surplus of amino acids which cannot be used for protein synthesis by animals ingesting such a protein, exerts no adverse effect. Within the limits usually encountered in diets composed of natural foodstuffs this is, for the most part, true. Since 1955, however, evidence has accumulated that under special conditions, such as in diets with a protein content inadequate to support maximal growth, a surplus of essential amino acids may actually display some deleterious effects. This situation has been called amino acid imbalance. The latter concept has been far less successful than that of amino acid balance, because an amino acid imbalance is difficult to assess accurately under adequate feeding conditions.

Deleterious effects of imbalanced amino acid supply

At a symposium held to mark the 10th anniversary of the Nutrition Research Institute in Giessen in 1967, the one of us (J.M.) made some basic remarks on this question (1). He pointed out, that recent developments had cast some doubts as to whether the concept of amino acid imbalance can be further ignored for all practical purposes and remain a merely academic matter. The fact is that today several essential amino acids are produced commercially, either by synthesis or by fermentation, at a cost which could allow amino acid fortification of the diet even in developing countries in the near future. In developing countries food companies may

promote the consumption of certain amino acids like vitamins. In this way, it cannot be denied that, amino acid imbalance may arise in the future among large sections of poorly nourished populations.

For this reason, it might be useful to discuss here again the problem of amino acid imbalances as an example of an intolerance to essential food constituents.

The concept of amino acid imbalance originated from observations made by Elvehjem et al. (2) when they found that the addition of gelatine or threonine to a 9% casein diet lacking niacine resulted in a severe depression of growth rate that was prevented by a supplement of niacine or tryptophan. As shown in Table 1, the growth rate of the groups fed the diets supplemented either by gelatine or by threonine was very much inferior to that of the group fed the unsupplemented diet. This was considered to be a result of an amino acid imbalance due to the addition of a non-balanced protein like gelatine or an essential amino acid like threonine. It was corrected by a small addition of either niacine or tryptophan. The effect was originally thought to be intimately linked with niacine deficiency; however, similar adverse effects of amino acid supplements were subsequently observed in experiments on a variety of dietary proteins with mice, rats, dogs, pigs, and chicks as experimental animals.

TABLE 1

EFFECT OF NIACINE AND TRYPTOPHAN (TRY) ON GROWTH OF RATS FED DIETS CONTAINING 8% CASEIN AND GELATINE OR THREONINE (THR) (3)

Additions to 8% casein diet, containing 0.3% DL-Methionine				
Gelatine %	DL - Thr %	Niacine %	L-Try %	Weight gain (g/2 weeks)
—	—	—	—	15
6.0	—	—	—	5
6.0	—	2.5	—	27
6.0	—	—	0.1	32
—	0.36	—	—	4
—	0.36	—	—	35
—	0.36	2.5	0.1	32

These effects can be produced regularly by adding a quantity of protein (or an amino acid mixture) lacking one indispensable amino acid to a diet that is low or moderate in protein content.

Similar effects have also been produced adding a small quantity of one or two essential amino acids to these diets. Amino acid imbalances are therefore of two types. The first type induced by the addition of a non-balanced protein will be discussed first.

An example of the creation of an imbalance of this type is given in Table 2.

TABLE 2

EFFECT OF AMINO ACID SUPPLEMENTS ON GROWTH OF RATS FED ON DIETS CONTAINING 87% RICE (3)

Supplements

L-Lys	DL-Thr	Other	Weight gain (g/2 weeks)
—	—	—	15
0.4	0.5	—	30
0.4	0.5	3% A.A. mix—Leu	22
0.4	0.5	3% A.A. mix+Leu	52

Indispensable amino acids in proportions in casein.

The addition of the first and second limiting amino acid in rice, namely lysine and threonine, doubles the weight gain. Supplementation of this diet with a non-balanced amino acid mixture lacking in leucine causes an imbalance resulting in growth depression which can be prevented by a small addition of the most limiting amino acid, namely the addition of a protein lacking in an essential amino acid is quite predictable. If the quantity of non-balanced protein or amino acid mixture in a diet is kept constant while the quantity of basal protein is increased, the effect of the non-balanced mixture becomes proportionately less, as shown in Table 3. However, if the quantity of the non-balanced mixture is also increased, the growth rate of animals fed higher levels of the basal protein is also depressed.

TABLE 3

EFFECT OF DIETARY PROTEIN ON GROWTH DEPRESSION RESULTING FROM AN IMBALANCE CAUSED BY ADDITION OF 3.5% OF A MIXTURE OF INDISPENSABLE AMINO ACIDS LACKING IN THREONINE (3)

Diet		
Casein %	Mixture	Weight gain (g/2 weeks)
6	—	22
6	+	5
8	—	45
8	+	31
15	—	85
15	+	83

We can conclude that the first mechanism of inducing an amino acid imbalance is not limited to low protein diets, but may well be released in animals on a diet providing enough protein for maximum growth. This does not appear to be the case with the second mechanism of causing an amino acid imbalance, namely by addition of a small amount of an essential amino acid or acids. For this second mechanism to be effective, the protein content should be relatively low.

An example of this type of amino acid imbalance has already been given in Table 1, where growth was almost completely depressed by the threonine addition. Another example is shown in Table 4, where the supplementation of a diet deficient in two amino acids in sequence is represented.

This experiment shows that the organism seems to be particularly sensitive to the balance between the first and second limiting amino acid on a low protein diet as in rice. A very slight excess of threonine over lysine as well as a very slight excess of lysine over threonine creates an imbalance with growth depression. It has already been stated that this second type of amino acid imbalance is rather difficult to predict. Usually, the amino acid causing the imbalance is the one that is second most limiting for growth.

Even an adequate protein content of a diet is not always sufficient to prevent an imbalance upon the addition of an amino acid. The basal protein must also be adequate quality-

wise and have its amino acids available in the proportions indicated by the chemical analysis.

TABLE 4

EFFECT OF LYSINE AND THREONINE SUPPLEMENTS ON THE GROWTH OF RATS FED A DIET OF 90% RICE (4)

Supplements		
L-Lysine HCl %	DL-Threonine %	Weight gain (g/5 weeks)
—	—	57
0.1	—	78
0.1	0.2	138
0.1	0.3	114
0.3	0.1	131
0.3	0.2	154

TABLE 5

EFFECT OF LYSINE ADDITIONS ON THE GROWTH OF RATS FED A DIET OF 10% ZEIN AND 10% GLUTEN SUPPLEMENTED WITH L-HISTIDINE 0.2%, L-TRYPTOPHAN 0.14%, L-THREONINE 0.08%, DL-METHIONINE 0.20% AND L-VALINE 0.16% (1)

L-Lysine HCl %	Weight gain (g/2 weeks)
—	8
0.150	23
0.300	36
0.450	41
0.600	48
0.750	35

If this is not the case, the situation is similar to that encountered in the first type of amino acid imbalance mentioned previously. We may indeed consider such an apparently adequate protein in which the availability of some amino acids is reduced, as composed of part of a certain amount of well-balanced protein and part of a non-balanced protein. In such diets, a high total protein content does not preclude the creation of an amino acid imbalance.

Even a diet with high protein content (40%) can be imbalanced. In case the imbalance of such a basal diet is not severe enough to cause growth depression per se, but is just marginal, a small excess of an essential amino acid may precipitate the appearance of an imbalance.

This shows once more how unpredictable the creation of an imbalance by addition of an amino acid is and demonstrates the need for testing such nutritional situations individually when it comes to amino acid fortification.

Having now discussed briefly the two main types of amino acid imbalance, we may give its definition as developed by Harper (3).

An *amino acid imbalance* is a change in the proportions of amino acids in a diet which results in a depression in food intake or growth rate that can be completely prevented by a supplement of the indispensable amino acid present in the least amount in the diet in relation to the amount required for optimal performance.

Not all adverse effects from dietary additions of individual amino acids should be grouped under "amino acid imbalance". Harper has tried to group the various adverse effects according to the apparent differences in the underlying causes. He distinguishes: 1) imbalance as defined above, 2) antagonism and 3) toxicity.

Amino acid antagonism: two examples of adverse effects of dietary excess of individual amino acids appear unique. These are effects of an excess of leucine and excess of lysine. These are classified as amino acid antagonisms because excess leucine depresses the utilisation of the structurally similar isoleucine and valine when the latter two are not limiting for growth and excess lysine depresses the utilisation of arginine. An amino acid antagonism differs from an imbalance in that the growth depression caused by an imbalance is prevented by a supplement of the most limiting amino acid, whereas growth depression due to an antagonism is not prevented by the most limiting amino acid, but by a structurally related amino acid.

A typical example of antagonism involving the branched chain amino acids is given in Table 6.

In this assay, growth depression was prevented by isoleucine and valine. However, it is not prevented by addition of

the most limiting amino acid, namely threonine (not shown in the table).

Amino acid toxicity: the effects of excessive intakes of individual amino acids that do not fit into the above categories of imbalance and antagonism are grouped under the general term toxicity until some meaningful basis for classifying them in another way is developed. Any adverse effect of an excess

TABLE 6

GROWTH-DEPRESSING EFFECT OF AN EXCESS OF LEUCINE AND ITS PREVENTION BY ISOLEUCINE AND VALINE (3)

Diet				
Casein*	L-Leu	DL-Iso	DL-Val	Weight gain
%	%	%	%	(g/2 weeks)
9	—	—	—	36
9	3	—	—	4
9	3	1.2	—	16
9	3	1.2	1.2	31

* Supplemented with 0.3% DL-meth. and 0.1% L-try.

of an amino acid which is not corrected by the addition of the most limiting amino acid nor by that of a structurally related amino acid will therefore be called toxicity. The quantity required to cause toxicity varies greatly among the individual amino acids, indicating, as suggested by Russel *et al.* that the basis for the effect is probably dependent on the structure and metabolism of the particular amino acid. Methionine, tyrosine, tryptophan and histidine, which enter into many metabolic pathways, appear to be the most toxic.

The deleterious effects which could be displayed by an unbalanced fortification of foods have been pointed out extensively in order to show that any addition of pure amino acids has to be done only on the basis of exact studies and calculations. Adding amino acids cannot be compared with adding table salt to a food nor even with putting some vitamins (at least ascorbic acid and the B-vitamins) on your meal. It will be very likely that amino acid fortification of foods will then come of age, as is the case for vitamins today. It will then be very important to remember that the margin between an

effective and a deleterious dose is very narrow for essential amino acids and depends on the composition of the basal diet, which is not the case for vitamins, at least not the water-soluble ones.

Fortification of food stuffs and diets

Large parts of the populations in many countries of the world are depending on cereal diets. Lysine is the first limiting amino acid. Since lysine addition doubles the protein efficiency of wheat, it would be theoretically possible to double the protein supply from wheat in the world. With a yearly wheat production of about 200 million tons, this corresponds to about 25 million tons of protein which could be spared by lysine fortification. This value is of the same order as the total annual world production of animal protein.

There are many publications on amino acid supplementation of human foods and diets. The FAO/WHO/UNICEF-Protein Advisory Group (PAG) collected a list of references in the non-medical field up to 1968. In this list the first paper—published already in 1951—is a report on studies about the enrichment of wheat bread by lysine or yeast, and we are very happy to find the name of one of us (H.-D.C.) among the authors of this early paper.

In the amino acid fortification of foods, two basic situations are encountered. Rosenberg (4) showed that five-week growth data of weanling male rats maintained on a diet of 90% dried commercial white bread supplemented with graded levels of lysine and having a protein content of 12.5%. With increasing amounts of essential amino acids, increasing gains were obtained until the optimum was reached. Supplementation with larger amounts did not bring about any particular change; growth had reached a plateau. This type of response is most common when food containing a substantial amount of protein is supplemented with the first limiting amino acid. The second type of response is found when the food contains a lower protein concentration, as in rice for instance. Supplementation with amounts larger than needed for optimum growth causes an imbalance and results in growth depression. The five weeks growth of weanling male rats on 90% precooked rice supplemented with graded levels of lysine and having a protein content of 7.75% shows an obvious imbalance creat-

ed by higher than optimum additions of the first limiting amino acid, lysine.

The peanut is one of the three major world oilseeds and a great potential protein source for humans because of its pleasant taste. Unfortunately, peanut protein is rather unbal-

TABLE 7

EFFECT OF AMINO ACID SUPPLEMENTS ON GROWTH OF RATS ON DIETS CONTAINING 10% PEANUT PROTEIN (1)

Supplements				
DL-Methionine %	L-Lysine HCl %	L-Threonine %	Weight gain (g/4 weeks)	PER
—	—	—	32	1.53
—	0.4	—	23	1.28
0.3	0.4	—	62	2.34
0.3	—	—	56	2.01
0.2	—	0.1	43	1.88
0.2	0.4	0.1	92	3.00

The danger of causing an imbalance is still greater when the second limiting amino acid is added without the first being adjusted, as already mentioned when the concept of amino acid imbalance was introduced.

How delicate the balance between first, second and third limiting amino acid might be is illustrated in Tables 7 and 8. The results are taken from a series of experiments in which one of us (J.M.) tried to establish the optimum supplementation of peanut protein in order to obtain a PER at least equal to casein.

TABLE 8.

EFFECT OF AMINO ACID SUPPLEMENTS ON GROWTH OF RATS ON DIETS CONTAINING 10% PEANUT PROTEIN (1)

Supplements				
DL-Methionine %	L-Lysine HCl %	L-Threonine %	Weight gain (g/4 weeks)	PER
—	—	—	30	1.55
—	—	0.2	26	1.35
—	0.4	0.1	23	1.37
0.3	0.4	0.1	110	3.29
0.3	—	—	64	2.16
0.3	—	0.1	59	2.06

anced and needs fortification with methionine, lysine and threonine for optimal performance.

Addition of the second limiting amino acid, lysine, causes an imbalance which is corrected by the first limiting amino acid, methionine. In the presence of methionine, the third limiting amino acid, threonine, creates an imbalance, which is in turn alleviated by lysine, but only by lysine plus methionine. Finally, the imbalance caused by threonine in the presence of the sole methionine, although less pronounced, is confirmed. This example demonstrates that the amino acid fortification of proteins, or diets for that matter, which show a multiple and not well profiled amino acid deficiency is not necessarily as straightforward as generally thought.

The most important thing is, of course, not to miss the first essential amino acid. This seems to be a truism, but may present some difficulties because amino acid composition data do not always reflect amino acid availability. At first sight, it therefore seems difficult to avoid errors causing imbalances. Fortunately, this danger is still rather remote in practice, because usually no single foodstuff is consumed exclusively as the sole diet except during extreme stress. Therefore, there is a need to carry out human studies to establish the beneficial effects of consumption of a diet containing cereals fortified with one or more of these amino acids.

Several authors have reported on the amino acid composition of different diets used in various countries. Just recently, M. Autret, Director Nutrition Division FAO, and some of his associates have published (5) an article "Protein value of different types of diet in the world: Their appropriate supplementation". On the basis of FAO —food balance— sheets out of 84 countries with 60 per cent of the world population (excluding mainland China) they described the amino acid supply by all these diets and graded them by using whole egg as reference protein. They found in these diets that based on balance-sheets isoleucine was the limiting factor 55 times, sulfur-containing amino acids 39 times, tryptophan 4 times, and lysine twice. Table 9 lists these data and shows that sulfur-containing amino acids and isoleucine also act as a secondary limiting factor, and valine and threonine as a third limiting factor. Numerous investigations on animals show that lysine, meth-

ionine-cystine, tryptophan and threonine really limit the protein efficiency of diets. By contrast, isoleucine and valine generally are not regarded as having a particular role in this field.

TABLE 9

FREQUENCY OF LIMITING FACTORS (5)

Limiting Factor	Iso-leucine	Methio. cystine	Lysine	Trypto-phan	Valine	Threo-nine
Primary	55	39	2	4		
Secondary	27	30	7	2	6	
Tertiary	3	10	9	4	46	11
	<hr/> 85	<hr/> 79	<hr/> 18	<hr/> 10	<hr/> 52	<hr/> 11

Therefore, it may be asked whether the protein of whole egg used as reference protein does not result in over-estimation of the importance of certain amino acids, especially isoleucine. The frequent role of methionine-cystine as limiting factor of certain notoriously satisfactory diets leads one to ask the same question in regard to sulfur-containing amino acids.

Although Autret and his associates were not able to find by calculation that lysine was the limiting factor in many diets, they did not doubt the need and usefulness of amino acid supplementation, esp. fortification of cereal diets by lysine. Pellet, however, in a paper on "Diets in the Near East" at the International Congress of Nutrition in August 1969 questions the usefulness of about 20 diets in the Near East and found —by chemical analysis and calculating chemical score— that only in a very few of these diets lysine was the limiting factor. He therefore suggested that lysine supplementation was a needless waste of money in most cases. But this author, however missed the following point:

1. He did not say that most of the people he was talking about consumed just those diets which he had found to be lysine deficient. So about 80% of the population were living on diets which had already proved to be deficient in lysine by calculation.

2. He overlooked an even more important point: In heat processed foods, especially in baked cereals, chemical analysis

says very little about availability of amino acids. This is particularly the case with lysine because the Maillard (browning) reaction effects especially the ϵ -amino group of this amino acid and decreases its availability. Only biological studies in animals or human beings are able to give a scientifically true reply to the question whether lysine fortification is of any value.

3. The chemical scores calculated by the author are based on egg protein that contains an excess of some essential amino acids (as mentioned above).

Numerous animal experiments have shown the useful effect of amino acid fortification. So the workers at the Central Food Technological Research Institute, Mysore, India, have undertaken a number of studies during the last few years both on experimental animals and growing school children to determine the supplementary value of a few selected amino acids on the protein quality of the cereal diets used in the experiments. With this background experience, the Indian Council of Medical Research formulated an integrated programme of research on the nutritive value of amino acid fortified cereals in Indian diets. If our memory is correct Dr. Gopalan has reported on the success of these human studies in one of the papers he presented in Prague at the Nutrition Congress in August 1969.

There are some studies that have been reported in which the addition of lysine to diets of school children or preschool children failed to show any beneficial effects. This could have happened easily when the caloric content of the diets was inadequate or when the supply of some other nutrients was insufficient. In some of these cases only by feeding supplemented wheat diets could weight gains or markedly greater weight gains be obtained by addition of certain vitamins and/or minerals and/or adjusting the caloric intake.

The FAO/WHO/UNICEF-Protein Advisory Group (PAG) dealt with the problem of amino acid fortification on several occasions. They discussed usefulness and feasibility of field studies under "real life conditions". Dr. Scrimshaw the director of the Department of Nutrition and Food Science, MIT Cambridge (Mass.) expressed the view on the basis of his experience with INCAP that whereas such an undertaking is clearly possible under hospital conditions, such demon-

strations may give false or negative results under field conditions where the food intake can be only partially controlled. His experience also indicated the difficulties of such tests. He felt that it would be difficult to demonstrate today that even the consumption of milk was beneficial. The burden of infections of various sorts places a major impediment in the way of obtaining clear-cut results. Dr. Sebrell, Director of the Department of Nutrition at Columbia University (New York), emphasized the difficulties which may result from unsuccessful tests, not necessarily indicating negative results, since these may discourage governments from supporting amino acid supplementation efforts even if their usefulness is strongly indicated by clinical and laboratory data.

In resolutions and recommendations the members of the PAG conclude:

There is growing interest among countries in the use of synthetic amino acids for the improvement of the protein quality of cereal grains and vegetable mixtures for human feeding.

The principle of amino acid supplementation of foods and feeds is well established and supported by extensive data from studies in animals. Metabolic studies in human subjects confirm the improvement in the net utilization of plant proteins and of protein mixtures, appropriate supplements with the limiting essential amino acids.

Hence, amino acid fortification is recommended when the protein quality of a food mixture for the supplementary feeding of young children can be improved significantly and economically by the addition of the principal limiting amino acid(s).

The effects of amino acid supplementation of cereal-based diets as an approach to the improvement of such diets deserves further exploration where it is likely that such supplementation could make a significant contribution at an economically justifiable cost. A careful analysis of the actual food consumed, particularly by the vulnerable members of low income groups, constitutes a necessary step in the identification of population groups where this supplementation could be considered.

The increasing availability at low cost of the most frequent limiting amino acids lysine and methionine, in the diets

of low-income populations, has increased pressures on governments to approve their use in the fortification of cereals. The choice of amino acid fortification, the addition of protein from fish protein concentrates, oil seed flour or both must be made on a combination of economic, nutritional and political grounds which are still controversial.

There was an article written on that problem by D. M. Hegstedt (6). The question has been looked at from different angles, and it ends very critically — with the statement: “Amino acid supplementation must be considered an expensive gamble that the developing nations can ill afford.” The argumentation of this article cannot be over-looked, especially because its author is one of the most outstanding nutritionists, the director of the Department of Nutrition, Harvard School of Public Health, and editor of “Nutrition Review”.

Dr. Hegstedt feels that most of the reports on that problem are overenthusiastic about the benefits which may be derived from the fortification of cereals and have either failed to consider or appraise adequately certain aspects of the problem.

He criticizes that the advocates of amino acid fortification as having too few doubts about feasibility, efficacy, and cost of the procedures recommended by them. He thinks that there is still a distinct possibility that amino acid supplementation will not be effective and that, if it is, it will be much too expensive for these countries to bear. Furthermore, if the problem is left in the hands of the enthusiasts, it is likely that it will be an accomplished fact before data are available to evaluate either the effectiveness or the cost relative to other procedures.

Dr. Hegstedt refers to economic calculations made by the authors of “The World Food Problem”, edited 1967 by the Science Advisory Committee of the President of USA. They estimate that optimal results would be obtained with the addition of 0.3% lysine and 0.15% threonine to white flour. These amino acids were assumed to be available at a cost of \$1.00 and \$1.50/lb, respectively. They compared these costs with those of supplying equivalent amounts of lysine as FPC (fish protein concentrate) and SBP (soybean protein), which were assumed to cost \$0.25 and 0.15/lb, respectively. These calculations indicated that the use of FPC would be 1.3 times more expensive and SBP 1.1 times more expensive than amino acids.

Dr. Hegstedt criticized that they failed to consider the fact that use of FPC or SBP would add protein as well as amino acids to the flour. A more appropriate estimate should include the total amount of protein in the product as well as the nutritional quality.

In a table given in Dr. Hegstedt's publication the protein content of the product multiplied by the efficiency with which it is used yields the percentage of utilizable protein. The cost divided by this value gives the apparent cost of the utilizable protein. Estimated in this way the cost appears similar for FPC and lysine plus threonine, if 5% FPC is added, and even less if 10% FPC is used (see Table 10).

TABLE 10

EFFECT OF SUPPLEMENTATION OF WHEAT FLOUR UPON THE
NUTRITIVE VALUE OF PROTEIN AND RELATIVE COSTS
OF UTILIZABLE PROTEIN (6)

	Protein Content	Relative Nutritive Value	Utili- zable Protein ^b	Cost, \$/100 lb	Cost of Utilizable Protein \$/lb.
Wheat flour	13.75	24	3.20	8.00	2.50
Wheat flour + 0.2% lysine—HCl	13.94	38	5.30	8.20	1.55
Wheat flour + 0.5% lysine—HCl	14.25	46	6.55	8.50	1.30
Wheat flour + 0.5% lysine—HCl + 0.3% threonine	14.55	56	8.14	8.80	1.08
Wheat flour + 5% FPC	16.66	42	7.00	8.85	1.26
Wheat flour + 10% FPC	21.26	50	10.68	9.70	0.91

FPC = fish protein concentrate.

^a Nutritive value relative to lactalbumin.

^b Protein content X RNV (relative nutritive value) = utilizable protein.

Dr. Hegstedt does not take into account other economic factors such as costs for transportation, admixture, storage and distribution which could be different depending on the mode of enrichment.

The PAG did not overlook this important point. In its Ad Hoc Meeting on "Amino Acid Fortification" (May 1969) the

PAG discussed this question on the basis of a working paper prepared by U. Kracht, an associate of Professor von Blankenburg, Berlin. The most important points of Kracht's paper should be referred to here. He starts from the hypothesis whether the cost of lysine fortification would be lower in comparison to any other method of cereal supplementation on the basis of equal results. This hypothesis is examined by the following considerations: a daily per caput cereal ration is fortified with lysine and compared to enrichment with various other protein foodstuffs. The calorie supply is kept constant at 2,000 calories for all rations by reducing the quantity of wheat according to the caloric contribution from the protein carriers. With each cereal group, the protein level is increased up to the approximately equal amount of utilizable protein.

On the basis of calculations published by the Dutch State Mines Kracht compares the supplementation of whole wheat, wheat flour (60-70% extraction rate), Bulgar (parboiled wheat), maize meal, polished, and parboiled rice with the following supplements: lysine, soybean flour, skim milk powder, meat, fish and fish protein concentrate (FPC), but the latter only 0.5% and not, as Hegstedt did, 5% or 10%.

The result of these comparisons verifies the hypothesis mentioned above with one major exception: the cost of protein enrichment of wheat flour with some 0.5% of fish protein concentrate (FPC) amounts to less than half of that of lysine fortification. In the case of polished rice, soybean flour appears to be economically more advantageous than lysine, its enrichment costs being only 76% of that of lysine fortification. It should be noted especially that soybean flour is much more economical than skim-milk powder. Groundnut and cottonseed flour would have to be added in considerably higher quantities as they are themselves deficient in lysine; this would result in higher cost.

It would not be justified to compare the relative costs only on the basis of protein enrichment, as all other protein carriers apart from lysine also provide vitamins and minerals, in which the diets of the needy populations are normally deficient, too. Therefore, a realistic comparison can only be based on enrichment cost for lysine plus adequate vitamin addition with the respective cost of other protein sources.

Thus, total enrichment costs including lysine, vitamins,

and minerals but excluding cost for admixture amount to 0.5 to 0.7 cents per caput and day or US \$1.83 to 2.56 per person per year. In case of using soybean flour, the respective cost would make up US \$2.56 to 2.92 (for polished rice only US \$1.38), which demonstrates that from the economic point of view there is only little difference between fortification cost for lysine and soybean flour.

Kracht emphasizes the point, that these calculations neglect two important factors: food acceptability and distribution and storage cost for the enrichment products. As to acceptability, the addition of 0.1 to 0.2% lysine neither affects the organoleptic qualities, nor the cooking or baking properties of cereals. An addition of some 6% of soybean flour to wheat flour may already affect flour acceptability. Furthermore the enrichment of 2 million tons of wheat flour would need some 120,000 tons of soybean flour versus some 4,000 tons of lysine, which would mean a tremendously higher amount of storage and distribution cost in the case of soybean flour.

The same is true for cottonseed or groundnut flour as possible supplements. For these also acceptability would pose a great problem as these flours would have to be added in larger quantities due to their smaller lysine content, which would change the properties of the basic cereal.

With regard to FPC enrichment, distribution costs could be considerably reduced, as on the basis of a 0.5% supplementation only some 10,000 tons of FPC have to be handled. Including these costs, enrichment with FPC could result in cheaper fortification cost than that of lysine. But contrary to Hegstedt's considerations — the cost will be considerably higher if the FPC supplementation is done by 5% or 10%.

Furthermore Kracht has pointed out that his calculations were based on a mere cereal diet. The actual increase, however, will depend on the quantity and quality of protein derived from other dietary components. If, for instance, the diets include a high proportion of pulses with high lysine contents, the nutritional effect of lysine fortification will naturally be lower. The whole problem is certainly not an easy one.

Coming to an end with my report I should like to refer

to a statement which is made in India on the future plans for studies in this field.

There is certainly a need to continue studies on the different aspects of the problem of lysine fortification. The need to expand these studies and to include other important amino acids such as methionine, threonine and tryptophan has been felt. If facilities and resources are available, work on these aspects will also be undertaken.

Amino acid fortification of a staple food or other foods appears to have become feasible from the economic point of view more information is urgently required on the effectiveness and health benefits of its practicable application under conditions of every day living obtaining in the developing countries of the world.

It is necessary to examine to what extent and in what areas or groups and by what channels the amino acid fortification programme could be implemented towards improving the protein quality of the diets of the affected population. Therefore — as the PAG has stated in January 1970 — the decision as to fortification of staple foods with amino acids will have to be made on a country basis. The target groups that can be expected to benefit should be identified and the desirability of amino acid fortification should be judged in comparison with alternative approaches to meeting national protein needs.

Undoubtedly, the whole problem of amino acid fortification is interesting and important from the theoretical as well as practical point of view.

RESUMEN

Fortificación con aminoácidos

Se discute el problema de la suplementación con aminoácidos desde diferentes puntos de vista y se expone la conveniencia de aumentar y mejorar el suministro de proteínas a vastos sectores de la población mundial. Se citan ejemplos de alimentos no balanceados de suplementos y se describe la posibilidad de efectos deletéreos. Los aspectos nutricionales y médicos son también analizados.

La fortificación con aminoácidos de los alimentos más comunes y de otros alimentos parece ser la medida más viable desde el punto de vista económico. Se requiere más información sobre la efectividad y beneficios para la salud que se obtendrían con su aplicación bajo las condiciones diarias de vida que predominan en los países en etapa de desarrollo.

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