

Diet Therapy



The Amino Acid Requirements of Adults

A REVIEW

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THE TERM protein, used to describe the nitrogenous substance found in body tissue, was coined from the Greek verb meaning "to take first place" and gives some indication of the importance that was early attached to that fraction of the diet.

It soon became evident that proteins differ in their value and that such differences are due to amino acid composition. The early protein studies of Osborne and Mendel and of other investigators have been thoroughly reviewed by Rose.¹ A little more than 20 years ago, Rose² reported on the qualitative and quantitative amino acid requirements for normal growth of the rat. The next step was to find that of the ten amino acids essential in the ration of the growing rat, eight must be furnished in the diet to maintain nitrogen balance in adult man. Finally, the amount of each that is required for that function of nitrogenous compounds was determined. The results of these laborious and extensive studies were first summarized in a publication in 1949.³ More recent studies of the requirements of women for the essential amino acids have been reported by Leverton and co-workers⁴⁻⁸ Swendseid and Dunn^{9,10} and by workers in the laboratories of the University of Wisconsin.^{11,12} The quantitative requirements of adult men and women as found in the foregoing studies are given in Table I.

The general plan of all of these studies using

human subjects was much the same. Subjects were fed a carefully controlled semisynthetic diet which provided generous amounts of the essential amino acids with additional nitrogen for the synthesis of the dispensable amino acids. Nitrogen balance was the criterion of adequacy. When the subjects had attained nitrogen balance on the "complete" amino acid mixture, the amino acid for which the requirement was being determined, was removed to produce a negative nitrogen balance and then replaced stepwise until balance resulted. Calories were provided in amounts sufficient to just avoid weight gain. It is of interest to note that as the subjects were changed from a diet of ordinary foods to the semisynthetic diet, it was neces-

TABLE I
Minimum Amounts of Essential Amino Acids Required for Maintenance of Nitrogen Balance in Adults

Essential amino acid	Women g/day	Men
Isoleucine	0.450	0.70
Leucine	0.620	1.10
Lysine	0.500	0.80
Phenylalanine with tyrosine present	0.220 0.900	1.10 —
Sulfur-containing amino acids	0.550	—
Methionine	0.290	1.10
Cystine	0.250	—
Threonine	0.310	0.50
Tryptophan	0.160	0.25
Valine	0.650	0.80

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sary in most cases to increase calories. In our own studies, an increase in calories of from 13 to 33 per cent or an average of 18 per cent was needed in order to attain nitrogen balance and prevent weight loss. Rose¹³ has reported a similar increase in caloric requirement.

The amino acid requirements of women appear to be somewhat less than those of men as reported by Rose. However, Clark *et al.*¹⁴ observed no striking difference in the quantities of lysine required by men and women for nitrogen equilibrium. The latter investigators report a statistically significant relationship of lysine requirement to body weight, surface area, creatinine excretion and metabolic size. These findings differ from those of Rose *et al.*¹³ and of Jones, *et al.*¹¹ who found no relation of requirement to body size. The requirement for lysine as reported by Clark *et al.*¹⁴ is greater than that reported by Rose³ for men or by Jones *et al.*¹¹ for women.

These requirements are basic to further research in this area. They represent laborious effort on the part of the investigators and real self-sacrifice by the subjects. In order that these results may be most valuable, it is important to recognize their limitations as well as their contributions. These determinations have been made on a small number of subjects, under carefully controlled conditions and for relatively short periods of time. Length of time on the experimental diet may be a factor that needs consideration. For example, it has been suggested by Nassett¹⁵ that histidine may not actually be a dispensable amino acid over a long period of time, but for a short period may be furnished by the degradation of hemoglobin.

The proposed requirements represent only the quantities needed to maintain nitrogen balance. There is no doubt of greater requirements for some other functions of amino acids. For example, Chaloupka, and co-workers¹⁶ working with rats and Vivian, and associates¹⁷ with human subjects, found that a lower intake of tryptophan was needed to maintain nitrogen balance than to form blood pyridine nucleotides. Greater differences probably exist in the requirements for growth, reproduction, antibody formation, and for the many other functions of amino acids in the body. Total calo-

ries, total nitrogen, previous diet, distribution of amino acids, and many other factors undoubtedly influence the requirements.

The limitations as well as the contributions of these studies of amino acid requirements have been discussed in a previous paper.¹⁸ Recognition of the limitations of available data is not intended to underestimate their value. They represent basic and fundamental information which, if properly applied, can contribute to the solution of many problems of protein nutrition.

Available data on the amino acid composition of self-selected diets²⁰ in this country and on the amino acid content of the "Average American Diet"¹⁹ indicate that problems of protein deficiency are not directly the result of an intake of the essential amino acids below the proposed requirements (Tables II and III).

TABLE II
Amino Acid Intakes of Women on Self-chosen Diets

Essential amino acid	Intake g/day		Minimum requirements of women for essential amino acids
	Women in nitrogen balance	Women in negative nitrogen balance	
Isoleucine	1.62-5.73	1.15-4.88	0.450
Leucine	4.83-7.35	3.37-6.25	0.620
Lysine	3.25-7.17	1.70-5.85	0.400
Methionine	0.83-2.54	0.67-2.03	0.290
Cystine	—	—	(0.250)
Phenylalanine	2.88	1.53-4.03	0.220
Tyrosine	—	—	(0.900)
Threonine	1.44-3.44	0.97-3.02	0.310
Tryptophan	0.44-1.28	0.25-0.91	0.160
Valine	3.20-4.58	2.51-5.98	0.650
Total nitrogen	8.20-15.20	4.50-14.40	10.000

From: REYNOLDS, M. S.: *J. Am. Dietet. A.* 33:1016, 1957.

We must keep in mind, however, the fact that the experimental diets furnished 6 to 10 g nitrogen/day as well as a generous intake of calories. A diet low in protein and possibly also low in total calories may easily meet the requirements for essential amino acids or even the Rose "safe levels" and still not furnish adequate total protein, through failure to furnish enough



TABLE III
Essential Amino Acid Content of the "Average"
American Diet Compared with the "Safe" Levels for
Men

Essential amino acid	"Average American" diet g/day	"Safe" levels for men
Isoleucine	4.2	1.40
Leucine	6.5	2.20
Lysine	4.0	1.60
Methionine	3.0	2.20
Phenylalanine	4.1	2.20
Threonine	2.8	1.00
Tryptophan	0.9	0.50
Valine	4.2	1.60

From: REYNOLDS, M. S.: *J. Am. Diet. A.* 33: 1016, 1957.

nitrogen for the synthesis of the so-called dispensable amino acids.

These data on amino acid requirements have provided a basis for describing a pattern for a provisional reference protein.²¹ Comparison of the amino acid composition of a protein with that of the reference protein has been proposed as a means of determining the biologic value of the protein and has been found to agree quite closely with biologic determinations. It is quite possible, however, that in some foods, the concentration of amino acids made available to the body as a result of *in vivo* digestion may not be the same as that found by analysis following drastic methods of hydrolysis. Biologic trials may be necessary to verify values based on calculations.

As the commercial preparation of certain amino acids at a low cost has become practical, the possibility of supplementing cereal proteins with amino acids to balance their deficiencies immediately suggests itself. Flodin^{22,23} has presented data showing how all common cereal proteins can be improved in this way. This proposal has some merit for a diet in which a large proportion of the total protein is furnished by cereals. The fortification of wheat proteins with lysine represents a practical application of the principle. However, the value or necessity of such supplementation in bread containing milk proteins, as included in the "Average American diet" remains to be demonstrated. By reference to

Tables II and III it may be noted that the self-selected diets of women and the "average American diet" furnish lysine in amounts from two to three times the Rose "safe" levels for men. Moreover, such a procedure should be approached with caution and should not be looked upon as opening the way for indiscriminate amino acid supplementation. Scrimshaw and associates²⁴ reported on the effects on nitrogen retention of supplementing a corn preparation with lysine, tryptophan, and methionine. Nitrogen retention improved with the addition of lysine and tryptophan but decreased when methionine was added. He suggested that the added methionine may have created some type of imbalance. "Whether or not the supplementation of diets with synthetic amino acids will prove practical and desirable can only be determined by fundamental studies to obtain data not now available."²⁴ The effects of imbalances of amino acids that may be created when availability of amino acids is not known have been reported by Elvehjem.²⁵

A statement on the "Supplementation of Dietary Proteins with Amino Acids" adopted in October 1956, by the Food and Nutrition Board of the National Research Council²⁶ says: "The imbalance of essential amino acids found in some dietary proteins cannot always be corrected by adding a single amino acid, the imbalance being the result of a deviation in several of the essential amino acids from an 'ideal pattern' needed by the body. Multiple supplementation is generally required. This type of supplementation is at present best achieved by mixed diets where one food protein supplements another. The benefits to be derived from amino acid supplementation are uncertain until our knowledge of the consequences of amino acid imbalance is more complete. The Food and Nutrition Board recognizes the potential value of proper supplementation with amino acids and the desirability of intensive study of this problem."

In conclusion, data on amino acid requirements represent basic information, upon which a wide range of additional studies can be based. The need is apparent for studies of the effect of other factors in the diet on amino acid requirements and for data on the requirements of

additional age groups. Information concerning the utilization of amino acids of foods is imperative before widespread use can be made of current findings. These investigations are laborious and expensive but should be undertaken as a contribution to solving the protein problems of the world.

REFERENCES

1. ROSE, W. C.: Nutritive significance of amino acids. *Physiol. Rev.* 18: 109, 1938.
2. ROSE, W. C.: The nutritive significance of the amino acids and certain related compounds. *Science* 86: 298, 1937.
3. ROSE, W. C.: Amino acid requirements of man. *Fed. Proc.* 8: 546, 1949.
4. LEVERTON, R. M., GRAM, M. R., CHALOUPKA, M., BRODOVSKY, E., and MITCHELL, A.: The quantitative amino acid requirements of young women. 1. Threonine. *J. Nutrition* 58: 59, 1956.
5. LEVERTON, R. M., GRAM, M. R., BRODOVSKY, E., CHALOUPKA, M., MITCHELL, A., and JOHNSON, N.: The quantitative amino acid requirements of young women. 2. Valine. *J. Nutrition* 58: 83, 1956.
6. LEVERTON, R. M., JOHNSON, N., PAZUR, J., and ELLISON, J.: The quantitative amino acid requirements of young women. 3. Tryptophan. *J. Nutrition* 58: 219, 1956.
7. LEVERTON, R. M., JOHNSON, N., ELLISON, J., GESCHWENDER, D., and SCHMIDT, F.: The quantitative amino acid requirements of young women. 4. Phenylalanine, with and without tyrosine. *J. Nutrition* 58: 341, 1956.
8. LEVERTON, R. M., ELLISON, J., JOHNSON, N., PAZUR, J., SCHMIDT, F., and GESCHWENDER, D.: The quantitative amino acid requirements of young women. 5. Leucine. *J. Nutrition* 58: 355, 1956.
9. SWENDSEID, M. E., WILLIAMS, I., and DUNN, M. S.: Amino acid requirements of young women based on nitrogen balance data. 1. The sulfur-containing amino acids. *J. Nutrition* 58: 495, 1956.
10. SWENDSEID, M. E. and DUNN, M. S.: Amino acid requirements of young women based on nitrogen balance data. 2. Studies on isoleucine and on minimum amounts of the eight essential amino acids fed simultaneously. *J. Nutrition* 58: 507, 1956.
11. JONES, E. M., BAUMANN, C. A., and REYNOLDS, M. S.: Nitrogen balances of women maintained on various levels of lysine. *J. Nutrition* 60: 549, 1956.
12. REYNOLDS, M. S., STEEL, D. L., JONES, E. M., and BAUMANN, C. A.: Nitrogen balances of women maintained on various levels of methionine and cystine. *J. Nutrition* 64: 99, 1958.
13. ROSE, W. C., COON, M. J., and LAMBERT, G. F.: The amino acid requirements of man. 6. The role of the caloric intake. *J. Biol. Chem.* 210: 331, 1954.
14. CLARK, H. E., MERTZ, E. T., KWONG, E. H., HOWE, J. M., and DELONG, D. C.: Amino acid requirements of men and women. 1. Lysine. *J. Nutrition* 62: 71, 1957.
15. NASSETT, E. S. and GATEWOOD, U. H.: Nitrogen balance and hemoglobin of adult rats fed amino acid diets low in L- and D-histidine. *J. Nutrition* 53: 163, 1954.
16. CHALOUPKA, M. M., WILLIAMS, J. N., JR., REYNOLDS, M. S., and ELVEHJEM, C. A.: Relative roles of niacin and tryptophan in maintaining blood pyridine nucleotides, nitrogen balance and growth in adult rats. *J. Nutrition* 63: 361, 1957.
17. VIVIAN, V. M., CHALOUPKA, M. M., and REYNOLDS, M. S.: Some aspects of tryptophan metabolism on low niacin intake. *Fed. Proc.* 16: 401, 1957.
18. REYNOLDS, M. S.: Amino acid requirements of adults. *J. Am. Dietet. A.* 33: 1015, 1957.
19. BLOCK, R. J. and BOLLING, D.: *The Amino Acid Composition of Proteins and Foods*, ed. 2. Thomas, Springfield, Ill., 1951.
20. REYNOLDS, M. S., FUTRELL, M. F., and BAUMANN, C. A.: Nitrogen balances and amino acid content of self-selected diets of women. *J. Am. Dietet. A.* 29: 359, 1953.
21. ALLISON, J. B.: Evaluation of dietary proteins. *Nutrition Rev.* 14: 129, 1956.
22. FLODIN, N. W.: The philosophy of amino acid fortification of foods. *Cereal Science Today* 1: 165, 1956.
23. FLODIN, N. W.: Amino acids and proteins. Their place in human nutrition problems. *J. Agr. Food Chem.* 1: 222, 1953.
24. SCRIMSHAW, N. S., SQUIBB, R. L., BRESSANI, R., BÉHAR, M., VITERI, F., and ARROYAVE, G.: Vegetable protein mixtures for the feeding of infants and young children; in *Amino Acid Malnutrition, XIII Annual Protein Conference*, Rutgers Univ. Press., New Brunswick, N. J., 1957, pp. 28-46.
25. ELVEHJEM, C. A.: Amino acid balance in nutrition. *J. Am. Dietet. A.* 32: 305, 1956.
26. Committee on Amino Acids: Statement on supplementation of dietary proteins with amino acids. *Proc. Food & Nutrition Bd.* 16: 41, 1956.