Soybean Protein in Human Nutrition: An Overview

V.R. YOUNG and **N.S. SCRIMSHAW,** Clinical Research Center, and Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA USA, and **B. TORUN** and **F. VITERI,** Institute for Nutrition for Central America and Panama, Guatemala City, Guatemala, CA

ABSTRACT

The nutritional value of processed soy protein in human protein nutrition is reviewed on the basis of growth, nitrogen balance and metabolic studies in infants, children, adolescents and adults. When well processed soy products serve as the major or sole source of the protein intake, their protein value approaches or equals that of foods of animal origin, and they are fully capable of meeting the long term essential amino acid and protein needs of children and adults. The significance of the sulfur amino acid content of soy protein for practical human nutrition is also examined. For young children and adults, under conditions of normal usage of soy protein, it is concluded that methionine supplementation of good quality products is unnecessary and possibly undesirable. For feeding of the newborn, the limited data available suggest that supplementation of soy-based formulas with methionine may be beneficial. However, the appropriate level of supplementation is considerably less than that suggested from results obtained in rat feeding studies. At total protein intakes that approximate current dietary protein allowances, well processed soy protein products can replace meat and fish proteins without reducing the utilization of dietary nitrogen in adults, and they can serve as nutritionally valuable protein sources in cereal-based diets for child feeding. The value of long term studies concerned with tolerance to and acceptability of new soy protein products in adults is emphasized, and favorable results with two isolated soy protein products are described. The data indicate that properly processed soy protein foods are well tolerated and of good protein value for humans of all ages.

INTRODUCTION

The role of the soybean as a traditional food item in diets of populations in Southeast Asia is well recognized. More recently, advances in food technology resulting in the development of a variety of edible soy products, including concentrates, isolates and extruded-expanded products, with characteristics that resemble specific types of meat, have resulted in increased soy consumption by populations of technically developed regions of the world. There are now a variety of food uses of soy that contributes to the protein nutrition of populations that have not hitherto utilized soy to a significant extent. Table I lists some of these uses of soy. For these reasons we have reviewed the potential of soy to contribute significantly to the protein intake of humans at all ages.

Emphasis is given to the topic of protein nutrition with particular reference to the nutritional value of soy-containing foods. Elsewhere in this conference the significance of soy is discussed in reference to mineral and lipid metabolism and nutrition. We (1,2) have reviewed recently these latter aspects, and others (3-6) have discussed previously the role of soy protein in human nutrition. In this paper we present an overview of the literature relating to the nutritional value of soy intakes that are quantitatively significant in relation to meeting the physiological need for dietary protein in humans. Our discussion includes a series of still unpublished studies on the nutritional value of soy isolates in children, conducted at the Institute of Nutrition of Central American and Panama (INCAP) and in adults at M.I.T.

Protein Quality Evaluation in Humans

General Considerations. Dietary proteins are needed for a variety of purposes including replacement of tissue and organ proteins due to continuous metabolic losses, the formation and growth of new tissues during development, pregnancy, lactation and recovery from pathological conditions. These needs are met by the indispensible (essential) amino acids and nonspecific nitrogen sources (dispensible amino acids) that comprise dietary proteins.

It is usually accepted that the concentrations or the availability of individual essential amino acids are the major factors in determining nutritive value of a food protein source. Conversely, the extent to which a given source of food protein is capable of supporting an adequate state of nutritional health will depend on the physiological requirements of the individual for essential amino acids and for total nitrogen. It has been estimated (Fig. 1) that the human infant requires a source of mixture of food proteins that is relatively high in concentration of essential amino acid and that with growth and development the needs for essential amino acids decline in relation to the total protein requirement (7,8). Because of these changes in amino acid requirements, Arroyave (9) has concluded that the nutritional quality of a protein will vary depending upon the age of the individual consuming it. Since all age groups are likely to experience an increased use of soy in their diets during the years ahead, and because plant proteins are thought to be limiting or deficient in one or more of the essential amino acids, such as lysine and tryptophan in common hybrid maize or sulphur amino acids in proteins of legume seeds, it is particularly important to assess the capacity of foods based on soy protein to meet the amino

TABLE I

Some Food Uses of Soy in Relation to Human Protein Nutrition

Use	
Alternative to milk-based formulas	Infants
Hypoallergenic Food	Infants and children
Vegetable protein mixtures	Preschool and school age children
Protein-enriched drinks	Children
Food Analogues, replacers and extenders	All ages
Traditional food item	All ages

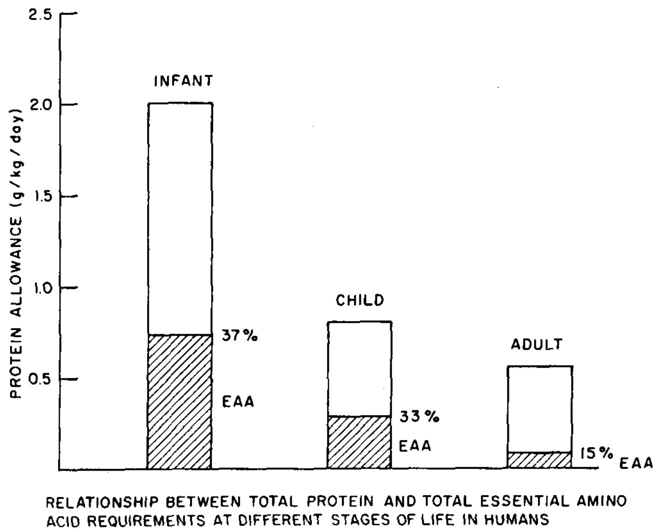

FIG. 1. Total protein allowance and proportion required as essential amino acids for humans at various ages. Based on FAO/WHO (7).

TABLE II

Summary of Observations with Soybean Protein in Feeding Studies with Experimental Animals[a]

1. Raw soybean meal reduces weight and dietary nitrogen utilization.
2. Steam heating improves the nutritional value of raw soybean meal.
3. Growth inhibitors are inactivated by heat.
4. Methionine supplementation markedly improves protein quality of soybean protein.
5. Other types of processes, such as toasting, increase protein quality of soybean.
6. Soybean flour *compliments* the nutritional value of cereal grains (corn, wheat).

[a]Slightly modified from Bressani (4).

TABLE III

Some Used or Potential Measures for Evaluation of Dietary Protein Quality in Human Subjects

Growth
Weight
Height
Lean body mass
^{40}K whole body counting
Body density
Body water (isotope dilution)
Creatinine Height Index (CHI)
Blood and serum constituents
Proteins: albumin, enzymes
Free amino acids
Urea N
Metabolic balance
Nitrogen excretion
Sulfur excretion

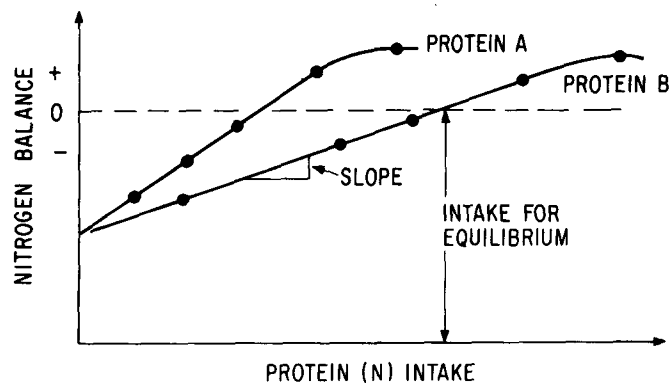

FIG. 2. An outline of the nitrogen balance response to changes in protein (N) intake, showing the various indices of N balance that are used for assessing dietary protein quality in human subjects.

acid requirements of human subjects of all ages.

Finally, since it is not always practical to measure the value of a protein directly for human nutritional purposes, a number of laboratory indices of protein quality have been developed. Chemical methods, although analytically precise, are subject to important limitations (e.g., see review ref. 10). Therefore, an alternative approach involves a biological assessment, as discussed in this conference by Satterlee.

Bressani (4) has summarized concisely the results of animal feeding studies with soy protein, and his summary is reproduced in Table II. The available data indicate that raw soybean is of low nutritional value in the rat and that its protein quality is improved by heat processing and by supplementation with methionine. The quantitative significance of these observations for soy protein in human nutrition must be evaluated carefully, and this is a major purpose of the following overview of results obtained in direct human studies.

Evaluation of Soy Protein Quality. Clinical methods for the evaluation of protein quality are based on the same principles applied to the corresponding animal assays, but require some modification for application to human subjects (11). The major procedures and criteria used are shown in Table III. These include growth or nitrogen balance, alone or in combination with biochemical analysis of serum proteins and amino acids, hemoglobin, blood urea nitrogen, and the urinary excretion of creatinine, sulphur compounds, and hydroxyproline. The majority of studies conducted in humans for determining the nutritional value of soy protein have been based on measures of growth, N balance and dietary N utilization in infants and children and on indices of N balance in adolescents and adults.

In nitrogen balance experiments with soy protein, the approaches followed and measurements usually made are depicted in Fig. 2. Studies may include several different intake levels of test protein and a reference protein source such as hen's egg, human or cow's milk. If multiple test levels of protein intake are studied, a determination is made of the relationship between nitrogen (protein) intake and nitrogen retention of N balance in each experiment.

Two different response criteria can be used to evaluate dietary protein quality from the N balance response curve (12) as depicted in Figure 3. The first involves an estimation of the efficiency with which dietary nitrogen is utilized. This is assessed from the *slope* of the nitrogen balance response curve in the region of the submaintenance-to-near-maintenance N intake level. Secondly, protein quality can be estimated in relation to how well a given protein source meets the requirement for total protein and amino acids, i.e., what minimum intake level of a given protein is required to maintain a zero nitrogen balance or body N equilibrium. In this case the response criteria is the *intercept* of the N balance response curve with the line of zero N balance.

These two approaches taken in the determination of protein quality are related but different. With either, dietary protein quality can be studied from the relationship of the N balance responses to the test protein in comparison to those obtained with the reference protein source (12). Alternatively, some studies have involved comparisons of N balance obtained with soy proteins and a reference

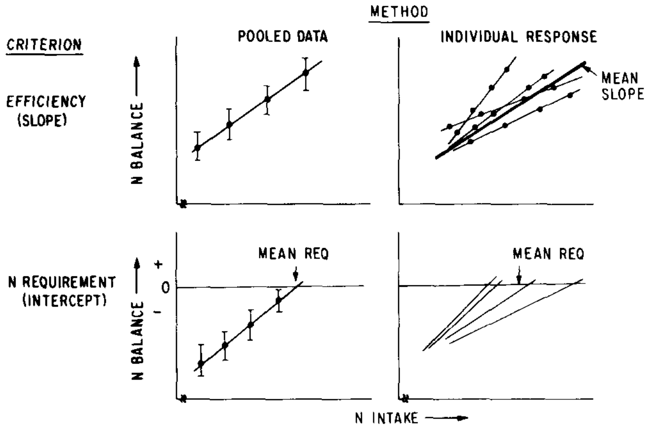

FIG. 3. Two N balance response criteria and methods of estimation for assessment of dietary protein quality in human subjects receiving graded intakes of test protein within the submaintenance-to-near-maintenance level of intake. From Young and Scrimshaw (1).

protein determined only at a single level of test protein intake. This approach can provide valuable information, but care must be taken in evaluating the results of such studies because the N balance response depends upon the particular level of protein intake chosen (13).

Growth studies are based on the same general approaches as those used in N balance experiments, but must be longer term studies. Because it is difficult to include a reference protein source and to control the dietary intake as precisely as in short term N balance experiments, interpretation of results obtained in growth studies is generally more difficult. However, such studies have provided a significant proportion of the information on the value of soy protein in infant nutrition.

Soy Protein Quality in Humans

Soy as the sole or major dietary protein source: growth studies in infants and children. Fomon and Siegler (14) have reviewed recently the available evidence concerning the growth of infants and children receiving soy as the sole or major source of essential amino acids and total nitrogen. A summary of the published studies in which growth, usually monitored as body weight gain, was a major response criterion is given in Table IV. Many of these studies involved use of commercial soy preparations which were supplemented with DL- or L-methionine. As shown in this Table, in nearly all of the studies linear growth and/or body weight gain of infants receiving soy equalled that obtained with cow's or human milk when direct comparisons were actually made. In other studies the growth rates achieved with soy-based preparations were judged, by the investigators, to be normal.

The results of earlier studies (18,23,24) and more recent unpublished data by this group (14), are included in Table IV. Growth responses with infants consuming a methionine supplemented soy protein isolate were found to be essentially the same as those receiving a milk-based formula. However, there appeared to be small differences in weight gain per unit of total energy intake. Infants receiving soy gained less per kcal formula ingested during the first four months of life than infants given milk-based feeds (14).

Overall, therefore, the results shown in this Table lead to the conclusion that soy flour and soy isolates are capable of promoting adequate growth of infants when they are either the sole or major source of protein in diets that also contain adequate levels of energy and other essential nutrients. It cannot be determined from this summary whether soy without methionine supplementation is utilized as efficiently as the methionine-supplemented product or a milk-based formula. Additional information on this point will be examined in more detail in a subsequent section.

Nitrogen balance studies in infants and children. Relatively few nitrogen balance studies have been conducted in infants and children receiving soy as the sole or principle source of dietary protein. A summary of the published studies is given in Table V together with indications of the test level of protein intake, age and number of subjects and major conclusion drawn from each N balance study. In summary, the available data indicate that N retention from methionine-supplemented soy isolates is apparently as good as that obtained with cow's milk. Because, as discussed earlier, the efficiency of N utilization depends, in part, upon the level of N intake, and the various studies have involved different test levels of soy protein intake, it is not possible to make a precise, quantitive statement about the nutritional value of soy proteins for infant and child feeding from the information given in Table V. Therefore, specific reference should be made to the recent investi-

TABLE IV

Partial Summary of Growth Studies with Infants and Children Receiving Soy as the Sole or Major Source of Food Protein

Protein type	Intake[a]	Subjects No	Subjects Age	Growth response and Comments	Ref
Soy isolate	?	20	Newborn	NG[b]; milk-based	(15)
Soy flour	2.5g/kg	58	Premature	Variable. birth-6mo	(16)
Soy isolate	?	30	Premature	NG	(17)
Full-fat flour (3105H)	1.7g/kg	4	4-6.5mo	NG	(18)
Soy isolate + M[c]	?	24	Newborn	NG; infant formula + solid foods	(19)
Soy isolate	?	34	Newborn	Growth ⩽ milk	(20)
Soy isolate + M; Soy flour + M; Soy flour	?	57	Newborn	Growth = milk	(21)
Soy isolate	?	29	2-15 mo	NG; infant formula	(22)
Soy isolate + M	6.5%	13	8-112 days	Growth = milk-based and breast fed	(24)
Soy isolate + M	6.5-15%	131	8-112 days	Growth = milk-based Slightly higher gain per kcal intake for milk-based	(24)

[a]Protein intake expressed as % of total calorie intake or g/protein/kg/day.
[b]NG = Normal Growth.
[c]+ M = diet supplemented with methionine.

TABLE V

Partial Summary of Nitrogen Balance Studies with Infants and Children Receiving Soy as the Sole or Major Source of Food Protein

Protein	Intake[a]	Subject No	Subject Age	N balance response	Ref.
Full-fat flour	1.7g/kg	4	4-6.5mo	=Milk	(18)
Soy isolate + M[b]	6.4-9.4%	4	23-30mo	⩾Milk	(25)
Soy extract	1.5-7g/kg	24	1-3 yrs	⩾Milk	(26)
Soy isolate + M	8-11%	8	8-120 days	=Milk-based	(14)
Soy isolate + M	12-16%	8	8-120 days		
Soy isolate + M	8-11%	8	⩾ 121 days	⩾Milk-based	(14)
Soy isolate + M	12-16%	12	⩾ 121 days	Good	(14)
Soy isolate + M	6.5%	6	113-118 days	Milk-based human milk	(24)
Soy isolate	0.8-2.0g/kg	8	~ 32 mo	~Milk	(27)
Soy isolate	0.5-1.25g/kg	8	~ 32 mo	~Milk	(27)
Soy flour	variable	14	3-7 yrs	80% Milk	(28)

[a]Protein intake expressed as % of total caloric intake or as g protein/kg/day.
[b]+ M diet supplemented with methionine.

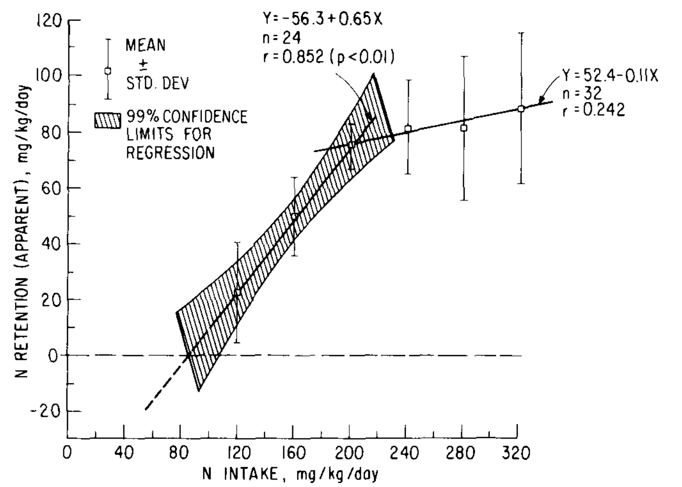

FIG. 4. Relationship between nitrogen retention and changes in nitrogen intake for children receiving a soy protein isolate (Supro-620) as the sole protein source. From Torun and Viteri (27).

gations by Torun and Viteri (27) in children who had recovered from protein-energy malnutrition. In these studies children received graded levels of intake of one of two soy protein isolates and the N balance responses compared with those obtained with milk as the reference protein. Figure 4 depicts results obtained with children receiving graded intakes of a commercially available soy protein isolate (Supro-620, Ralston-Purina Company, St. Louis, MO). As shown here, N retention increased linearly with increases in N absorption (or intake) up to 190 mg/kg/day, and thereafter N retention remained relatively constant. Therefore, Torun and Viteri (27) examined the N balance responses in children to each of two soy protein isolates in children receiving test protein intakes ⩽ 190mg N/kg/day. Table VI presents their N balance data for the two soy products, and they are compared here with data observed in similar studies with milk protein. From these results it is apparent that the nutritive value of the soy isolates approximates 86-107% of milk, depending upon the specific method of comparison. Thus, the nutritive value of the isolates tested in young children was essentially equivalent to that of milk protein.

Studies in Adults. We (1,2) have reviewed studies on the nutritional quality of soy protein in adults and summarized the results of a series of nitrogen balance experiments in young adult male subjects who were studied at several different test protein level, in our laboratories at MIT.

Figure 5 summarizes the N balance response data obtained when young adult men received egg (7 subjects) or a soy protein isolate (Supro-620) (8 subjects) at several levels within the submaintenance-to-maintenance range of total dietary protein intake. Table VII summarizes the various estimations of the nutritive value of soy based on an analysis of the N balance data (Fig. 5) using the approaches and criteria discussed above. The nutritional quality of the soy protein isolate is high, for healthy adults, approximating 80% of the value of egg protein in this experiment. The true digestibility (97%) of the soy isolate also was high and comparable to egg protein.

The slightly lower quality of the soy isolate may be due largely to its lower sulphur amino acid concentration relative to egg protein. However, in relation to practical human nutrition, it is important that the protein value of the soy isolate in adult humans is considerably higher than that suggested by feeding studies in rapidly growing rats. This point is discussed in more detail below.

A limitation of these and other studies (1) in adults is that they were of relatively short duration. In view of the trend toward an increase in the use of soy in the diet of

TABLE VI

Comparative Results of Nitrogen Balance Studies with Soybean Isolates and Milk, at Intake Levels ⩽200mg/kg/day[a] in Children

	Regression coefficient between N retention and: N intake	Regression coefficient between N retention and: N absorbed	N equilibrium attained with N intake of	Compound (mean) score relative to milk
Whole milk[b]	.64	.73	84	
Isolate 620	.65 (101)[c]	.70 (96)	86	98
Isolate 710	.59 (92)	.63 (86)	59	107

[a]N intake, absorption and retention expressed as mg/kg/day.
[b]Source: F. Viteri & R. Bressani, Bull World Hlth. Org. 46:827 (1972).
[c]Figures in parenthesis; % relative to milk (27).

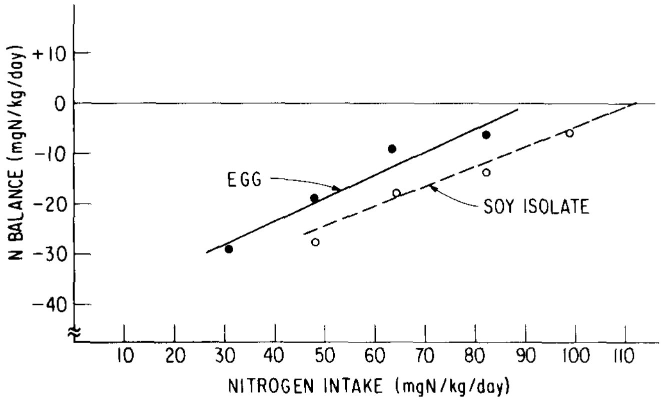

FIG. 5. Mean nitrogen balances in young adult men receiving graded intakes of egg (seven men) or soy protein isolate (Supro-620) (eight men). Lines fitted by least square analysis. Unpublished M.I.T. study.

TABLE VII

An Evaluation of the Protein Quality of Soy Protein (Supro-620), Relative to Egg Protein, in Adult Men[a]

Response criterion	Term	Method of estimation: Pooled data	Method of estimation: Individual response
Efficiency (Slope)	RVP	87	77
Requirement (intercept)	RNR	80	79

[a]Based on seven subjects with egg and eight with Supro-620.

$$RVP = \frac{\text{Slope with Supro-620}}{\text{Slope with egg}} = \text{Relative Protein Value}$$

$$RNR = \frac{\text{Mean N requirement with egg}}{\text{Mean N requirement with Supro-620}} = \text{Relative Nitrogen requirement}$$

adult populations, we considered it important to extend our observations to a controlled, longer term metabolic experiment in healthy adults. Therefore, eight young adult men were studied for the longer term capacity of a soy isolate (Supro-710) to maintain parameters of protein nutritional status. The experiment consisted of an 84-day N balance study and the diet provided protein entirely from the soy isolate, at level of 0.8 g protein/kg/day. From the results of short term N balance studies, this level was predicted to be sufficient to cover the protein needs of most young men. The results for N balance, body weight changes and whole body potassium, as a measure of protein mass, are summarized in Table VIII. Six of the eight subjects remained in N balance or equilibrium throughout this

TABLE VIII

Body Weight Changes, Whole Body Potassium Changes and N Balance in Eight Young Men Receiving, for 84 Days a Formula Diet Based on Soy Protein[a] (0.8 G Protein/Kg/Day)[b]

Subject	Weight change (kg)	N balance (mg N/kg/d)	Body K changes (*P*)
DK	4.7	10.8	NS
JD	+0.4	-6.1	NS
TK	-0.7	4.1	NS
JP	-4.8	-8.3	NS
BF	4.2	18.7	$P<0.05$
DT	-0.8	1.0	NS
RP	2.2	4.2	NS
AK	-1.8	1.4	NS

[a]Soy Isolate—Supro 710.
[b]Unpublished M.I.T. data (Wayler, Scrimshaw and Young).

TABLE IX

Concentration of Plasma Cholesterol Fractions in Young Adults during a Long Term Metabolic Study in Which They Received 0.8 G Soy Protein/Kg/Day

Cholesterol fraction	Normal diet	Soy diet[a]	Difference (p)
HDL	48.5 ± 17.5[b]	44.4 ± 10.8	NS
LDL	90.0 ± 15.9	76.9 ± 17.5	<0.025
VLDL	7.3 ± 5.0	6.3 ± 2.9	NS

[a]After 10 weeks with the experimental diet. Unpublished M.I.T. date (Wayler, Scrimshaw, and Young).
[b]Values expressed as mg/dl. Mean ± SD for 8 subjects.

long term study. For one subject (JP), the negative balance was probably causally related to an inadequate energy intake and for the other subject (JD), an inflammation of the knee associated with an earlier idiopathic chondromalacia may have been responsible for his negative N balance. Also, as summarized in Table IX, the concentrations of various cholesterol fractions in plasma were less at the end of the 84-day period of consuming soy as the sole protein source, compared with the values observed when subjects were consuming their usual diets. Although the lower cholesterol levels may be due to the changes in source of dietary fat in the experimental diet, the observations lend support to the view that diets consisting predominantly of vegetable proteins may reduce plasma cholesterol levels (29,30).

Findings of this long term metabolic study support the conclusion that the soy protein isolate is capable of maintaining the protein nutritional status of healthy young men.

Sulfur amino acid content of soy protein in relation to human protein nutrition. Experiments with the young, rapidly growing rat show clearly that the S-amino acids are the most limiting essential amino acids in soy and soy protein isolates and that their nutritional value is signifi-

TABLE X

Summary of Studies on the Effect of Methionine Supplementation on the Utilization of Soy Protein in Infants, Children and Adolescents

Protein	Intake[a]	Subject: No	Subject: Age	Response to Methionine	Author
Soybean	5-6%	2	21-23 mo	Improved N retention	(31)
Soy isolate	4%	3	6-15 mo	Improved N retention	(31)
Soy flour	7%	1	19 mo	Improved N retention	(31)
Soy isolate	9.3%	10	Newborn	Wt. gain (4 mo) same as unsupplemented Some differences.	(14)
Textured protein	0.6g/kg	9	13-17 yr	Improved N retention	(32)

[a]Protein intake expressed as % of calories of g protein/kg/day.

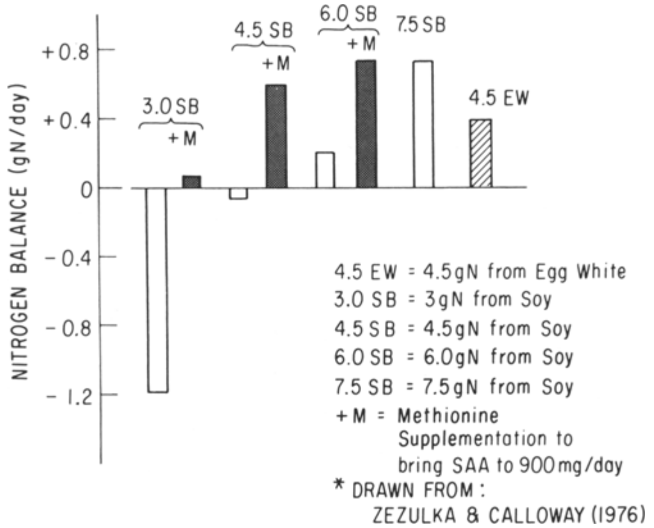

FIG. 6. Nitrogen retention in young men receiving soy, with and without methionine supplementation, at various soy intakes, compared with egg white. Drawn from data of Zezulka and Calloway (34). Total diet supplied 9 g N daily.

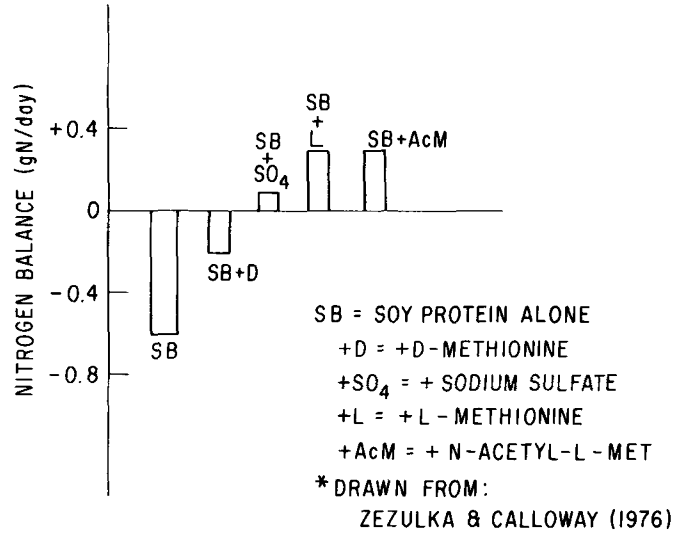

FIG. 7. Mean nitrogen balance in young men receiving 4.5 g N from soy protein isolate alone or supplemented with various sources of S-containing compounds. Drawn from data of Zezulka and Calloway (35).

cantly enhanced following methionine supplementation (4). It is important, therefore, to consider results of various human studies concerned with the nutritive value of soy, its methionine and cystine content, and the effects of methionine supplementation.

Table X summarizes results of some earlier studies on the effects of methionine supplementation on N balance or growth conducted in infants, children and adolescents.

On the basis of the studies summarized here and of studies by Kies and Fox (33) and Zezulka and Calloway (34), methionine supplementation improves N retention when low test intakes of soy protein are studied. Thus, Zezulka and Calloway (34) were interested in assessing the minimum amount of soy protein required to meet amino acid needs in adult men, when consuming a diet supplying an adequate level of total nitrogen, and the effects of supplementing soy with methionine on N utilization. The results of this study are depicted in Fig. 6. They show that with methionine supplementation, to bring the total daily S-amino acid intake up to the 900 mg level, the amount stipulated by the 1973 FAO/WHO Committee on Energy and Protein Requirements (7) to be sufficient for a 70 kg adult subject, the utilization of the soy protein isolate was improved at low intakes of test protein. However, at intakes of 6.5 g N per day from soy, nitrogen balance was similar to that achieved with 4.5 g egg white nitrogen (about 0.4 g protein/kg/day), and the methionine requirements appear to have been met with this intake of soy protein. These results indicate that this soy protein product was fully capable of meeting the amino acid requirements of adult subjects, without supplementation with methionine. However, at low intakes of the protein, supplementation with methionine improved the utilization of this soy protein, making it possible to meet the requirement for all of the other essential amino acids.

The use of crystalline methionine to supplement proteins limited in S-amino acids presents a number of problems and difficulties, including the development of unacceptable flavors due to methionine degradation. Hence, Zezulka and Calloway (35) also compared, as shown in Fig. 7, the capacity of N-acetyl-L-methionine (AcMet), which is not degraded during processing, to substitute for L-methionine in the supplementation of soy. Their results indicate that AcMet is as beneficial as L-methionine and also that sodium sulfate was partially effective in increasing N retention. The efficiency of AcMet in adult human subjects parallels results of studies in rats showing that it is nutritionally and metabolically equivalent to L-methionine (36,37) and at very high intakes it may be less detrimental, in terms of reduced rat growth, than L-methionine (38).

We have also assessed the effects of methionine supplementation on the utilization of a soy protein isolate in adult men. In the first study, methionine supplementation was given to about equal (supplementation at 1.1% of total protein) or somewhat exceed (1.6%) the level of total S-amino acid in the 1973 FAO/WHO Provisional Amino Acid Scoring Pattern (7). This pattern provides 3.5% total S-amino acids. In addition, the effect of a lower level of methionine supplementation was tested since it was desirable to know the minimum level of supplementation necessary to achieve a maximal N balance response in adult subjects. This study was conducted at a level of test protein intake of 0.51 g soy protein/kg/day, chosen to approximate the mean requirement for good quality egg protein (e.g., see Fig. 5).

The results of this first study, depicted in Fig. 8, agree with the observations of Kies and Fox (33), and Zezulka and Calloway (34), that methionine supplementation improves dietary N utilization in adults when soy is consumed as the sole source of protein at a deficient level of total N intake. It was apparent, however, that there was considerable variability in the N balance response to methionine supplementation among the subjects. This was also the experience of Zezulka and Calloway (34). With the highest level (1.6%) of methionine supplementation, a *deterioration* in overall nitrogen balance occured. This latter response parallels that reported in a series of earlier studies in young children concerned with effects of amino acid supplementation of corn and wheat on nitrogen retention (40-42). Not only did the addition of methionine fail to improve N balance when corn or wheat provided the entire source of dietary protein in these studies, but addition of methionine to corn masa protein resulted in a decrease in nitrogen balance. From these observations, N utilization in children is determined, in part, by the dietary balance of essential amino acids, and a disproportion in the amino acid pattern can adversely affect dietary protein quality. Our study also indicates that at marginal or deficient levels of total N intake, healthy young men may react negatively to relatively small imbalances among some of the dietary essential amino acids.

A second study was conducted to confirm and evaluate

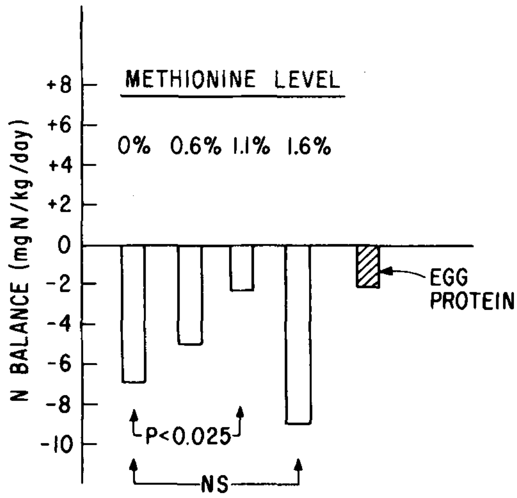

FIG. 8. Mean nitrogen balance in young men given a soy protein isolate (Supro-620) supplemented with various levels of L-methionine. Supplementation expressed as a % of total protein intake (which was 0.51 g protein/kg/day for all groups, including the egg protein control diet). The 1.1% level increased to total S-amino acid content to the level contained in the 1973 FAO Provision Amino Acid Scoring Pattern (i.e., 35 mg total S-amino acids per g protein). Unpublished M.I.T. study.

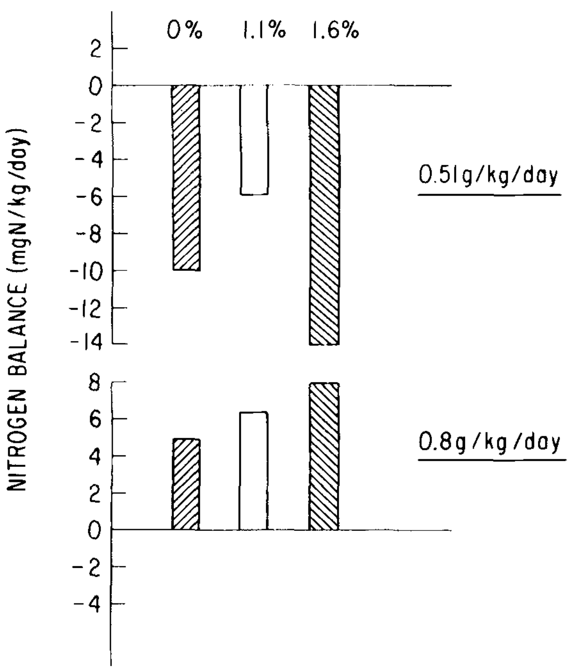

FIG. 9. Mean nitrogen balances in young men given two levels of a soy protein isolate (Supro-620) as the entire source of dietary nitrogen. Methionine supplementation was studied at levels equivalent to 1.1 and 1.6% of total protein intake. Unpublished M.I.T. study.

further the effects of L-methionine supplementation of soy protein. Two levels of methionine supplementation, equivalent to 1.1% and 1.6% of total soy protein intake, were studied for protein intakes of 0.51 g (about 5.6 g N/day) and 0.8 g protein/kg/day (about 9.4 g N/day). The results are shown in Fig. 9. For the lower protein level, N balance improved with the 1.1% level of supplementation in six of the eight subjects, and there was a reduction in N balance with the 1.6% level of supplementation in these same subjects. The other two subjects showed an improvement in N utilization with the 1.6% level. As also shown in Fig. 9, when soy intake was equivalent to 0.8 g protein/kg/day, the two levels of methionine supplementation had no effect on

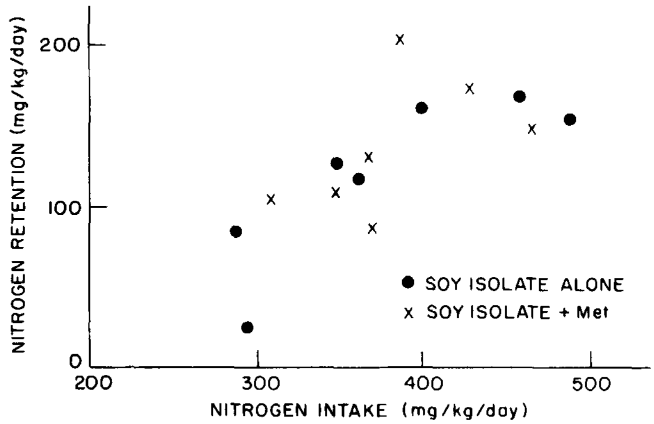

FIG. 10 Retention of nitrogen as a function of nitrogen intake by infants receiving a soy isolate-based formula with or without methionine supplementation. Taken from Fomon and Ziegler (14).

N utilization.

This second study confirms that methionine supplementation improves N balance when the level of soy protein intake supplies a limiting intake of S-amino acids, and that an adverse response may occur with levels of methionine supplementation which do not greatly exceed that estimated to meet the S-amino acid need per unit of total N intake. The metabolic basis for this adverse effect is unclear. However, at any of the supplementation levels tested, there was no measurable effect of methionine supplementation when the level of soy intake (0.8 g protein/kg/day) was sufficient to meet the dietary allowance for total protein in young adults (43).

A more important question concerns the extent to which soy proteins may be limiting in S-amino acids for infant and child feeding at normal levels of intake. The available data are limited, but results of the studies by Torun and Viteri (27) indicate that for children the sulfur amino acid content of soy isolates is adequate to promote N retention and growth.

Fomon et al. (44) have recently described results of careful growth and N balance experiments in normal, full term infants fed a soy isolate formula providing 2.25 g protein/100 kcal, to determine the effect of methionine fortification of the soy isolate in infant feeding. Although the N balance determinations (Fig. 10) failed to indicate any differences in performance between unsupplemented and methionine-supplemented soy-based formulas, these investigators did observe differences or trends in several other parameters.

In infants fed the unsupplemented formula, there was a statistically lower weight gain per 100kcal of formula consumed than in previously studied infants fed soy-based or milk-based formulas. Serum albumin concentrations were less at 28 days than in breastfed infants. Serum urea N was significantly higher than in infants receiving the same formula supplemented with methionine. The data thus showed that infants given the unsupplemented soy formula performed slightly less well during the first 6 weeks of life than breastfed infants and infants fed other formulas. Although it is difficult to judge fully the health significance of the findings by Fomon et al. (44), they suggest that methionine may be limiting in soy protein for infant feeding.

Although various other studies indicate that unsupplemented soy protein can be consumed at levels sufficient to correct and prevent infantile malnutrition (e.g., 26) a case could perhaps be made for a modest level of methionine supplementation of infant formulas that are based entirely on soy. As Fomon (45) has pointed out, as many as 10% of infants in the U.S. may receive soy-based formulas for

TABLE XI

Sulfur Amino Acid (SAA) Requirements of Rats and Humans, Together with SAA Content and Per Values of Two Soy Isolates

	SAA requirement (or content) (mg/g protein)	PER Values[a]
Rat		
Growing	50[b]	Supro-620; 1.65 + Methionine; 2.44
Adult	9[c]	Supro-710; 1.7 + Methionine; 2.4
Human		
Infant[d]	29	
Child[d]	34	
Adult[d]	24	
Soy Isolates[e]		
Supro 620	26	
Supro 710	26	

[a]Adjusted to PER 2.5 for Casein. Data provided by F. Steinke, Ralston Purina Co.
[b]From, Rama Rao et al. (46).
[c]Said and Hested (47).
[d]From: FAO/WHO (7).
[e]Ralston-Purina Co., St. Louis, MO.

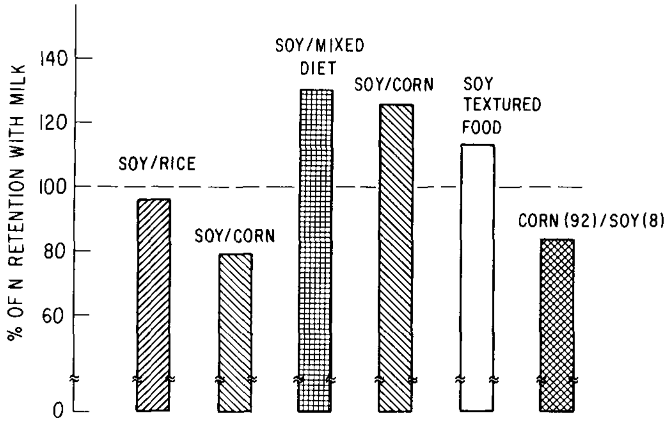

FIG. 11. N retention in children receiving soy-cereal diets, expressed in relation to N retention with milk. Drawn from summary of Bressani (5) and based on data of Chen et al. (48) for soy/rice; Dutra and de Souza (50) for soy/corn; Bressani et al. (52) for soy-textured food and Viteri et al. (53) for corn (92)/ soy (8) mixture.

prolonged periods and at a time when growth and development should proceed uninterrupted. Thus, it may be desirable to consider a modest level of methionine supplementation for this age group. For individuals aged about 1 year and above, however, we conclude that there is little nutritional or public health justification for supplementing soy protein products with methionine, particularly when soy is consumed as part of a diet of mixed proteins where the S-amino acid content is not likely to be a limiting factor.

With reference to methionine supplementation and infant feeding, it is apparent that the requirement for the sulfur amino acids expressed per g protein are considerably higher for the growing rat than for the infant and child (Table XI). Because of this it is to be expected that methionine supplementation would have a greater effect on the nutritional value of soy isolates for the rat than for the child. The PER data from studies with rats given in this table and the N balance and growth studies in infants and children support this prediction. This also suggests that it is not rational to use only PER values determined in the growing rat to regulate, in quantitative terms, the nutritive value of food protein sources for human consumption.

Soy in Cereal-Based Diets. An important contribution of soy in human nutrition is its use as a component of diets consisting of mixed protein sources. Therefore, soy has been studied in combination with other foods, particularly in cereal-based diets when given to children. The results of these various investigations are depicted in Fig. 11, based on the summary presented recently by Bressani (5). It can be seen that the nutritive value of soy in combination with rice, or corn flour, or with mixed sources such as milk solids and corn meal (54), as well as with oat flour (55), closely approaches that of milk. These findings, discussed in more detail by Bressani (5), indicate that when soy is incorporated with other foods, particularly cereal grains, the overall protein quality of the diet is high, and it is similar to that for good quality animal protein sources.

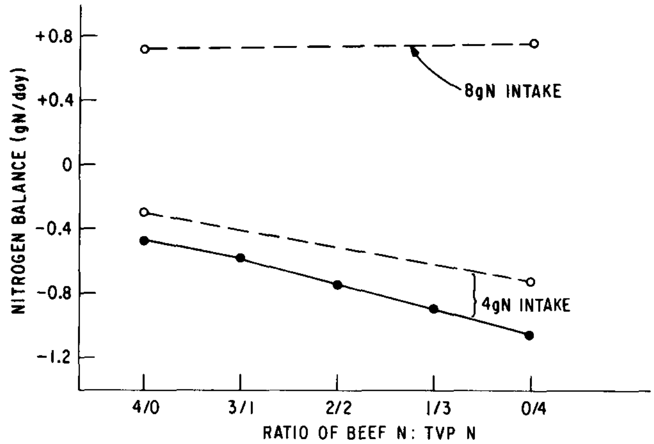

FIG. 12. Nitrogen balance in young adults receiving beef, or an extruded soy protein product (TVP) alone or in various combinations. Taken from Kies & Fox (39) and based, in part, on data of Kies and Fox (33).

Protein Quality of Soy-Beef and Soy-Fish Combinations. The use of soy protein concentrates (about 70% protein) and of soy protein isolates (90% protein), produced from defatted soybean flakes in processed meats and in texturized products (56,57), is another potentially important role of soy in human nutrition. Therefore, the nutritive value of soy in combination with meat or fish must be considered.

Kies and coworkers (32,33,39) have reported that at limiting N intakes, in adolescent boys and young adults soy protein has a lower nutritive value than beef. Thus, it is important to explore the extent to which soy may substitute for beef protein without an overall effect on the utilization of the dietary protein. Therefore, Kies and Fox (39) measured the effect of different dietary ratios of beef protein to extruded soy protien (TVP) on nitrogen utilization in eight young adults. Their subjects received an intake of 4.8 g nitrogen per day with a series of diets providing ratios of beef/soy N of 4:0, 3:1, 2:1, 1:3, and 0:4. The results are depicted in Fig. 12. Nitrogen balances of -0.44, -0.56, -0.75, -0.90, and -1.11, g N/day, respectively, were obtained for the foregoing dietary ratios of beef to soy nitrogen. Hence, these data indicate a linear decrease in protein value of the diet with increasing soy replacement of beef protein. However, in an earlier study by these investigators (33), there was no difference in N utilization of beef and soy when the test protein intake level was 8.0 g N/day (about 0.7 g protein/kg/day). These results are also included in Fig. 12. It must, therefore, be concluded that the effects of various beef-soy combinations on N utilization depend on whether the measurements are done at adequate or inadequate levels of protein intake. The results would also depend on the nutritional quality of the specific food tested, which, in turn, is influenced by the specific processing conditions used in producing the soy product.

TABLE XII

Summary of N Balance Data and Protein Quality Indices in Soy-Beef Replacement Study[a]

% Soy	100	75	50	25	0
% Beef	0	25	50	75	100
N balance[b]	-2.3	-3.2	-0.9	-1.1	-1.7
BV[c]	53	52	55	53	53
Digestibility (%)	97	99	98	98	98

[a]None of the diets showed significant ($p>0.05$) differences.
[b]mg N/kg/day.
[c]Biological value.

TABLE XIII

Summary of Preliminary Results on the Evaluation of a Soy Protein Isolate Alone and in Combination with Fish in Young Adult Japanese Adult Men[a]

Protein	N intake for requirement (mg N/Kg/day)	RNR[b]
Fish	87	
Supro-620	118	74
Supro/Fish (50:50)	91	96

[a]From Inoue et al. (59).
[b]RNR = Relative Nitrogen Requirement. (see Table VII).

For these reasons, we carried out a study to determine the extent to which the high quality soy isolate (Supro 620) could replace beef protein without significantly influencing overall dietary N utilization. For this purpose, a single test level of 0.6 g protein/kg/body weight/day was given. This was chosen on the basis of a previous study indicating this to be the amount of beef protein necessary in short term balance studies to meet the nitrogen needs of most young adults (58). Various combinations of beef and soy were tested, incorporating the soy protein into a commercially prepared bologna product.

A summary of the N balance data obtained in this study is presented in Table XII. Although significant ($p<0.05$) variability was found in nitrogen balance among the subjects, there were no significant differences in nitrogen balance among the various combinations of beef-to-soy protein. Thus, we conclude that a soy product of this quality, when given at a level sufficient to meet the protein allowance with beef protein, can replace beef without altering the protein value of the diet.

It should be emphasized that in our study, a 0.6 g/kg/day level of test protein intake was given equivalent to about 42 g protein/day for a 70 kg man, compared with ca. 30 g protein/day given to subjects by Kies and Fox (33). This is presumably the major reason for the differences in results obtained in the two studies, but a difference in the nutritional quality of the soy products tested cannot be ruled out.

Inoue et al. (59) have explored the nutritional quality of a soy protein isolate when mixed with 50% fish protein in studies in Japanese young men. Utilizing an approach similiar to that followed in our studies with MIT students (e.g., Fig. 5 and Table VII), Inoue et al. (59) estimated the intakes of fish protein and soy isolate alone or an equal mixture of fish protein and soy protein isolate necessary to maintain N balance in their subjects. The preliminary results of these studies given in Table XIII show that the protein value of the soy isolate-fish protein mixture is essentially the same as that of cod fish protein alone. These findings indicate that a soy product of this quality can replace at least 50% of fish protein without a change in the protein value of the diet.

TABLE XIV

Design of a Six-month Acceptability Study with a Soy Protein Isolate (Supro-620)

Design	
Subjects:	40 adult subjects (18 subjects—experimental group; 22 subjects—control group)
Diets:	Experimental—40 g soy protein isolate (Supro-620) daily
	Control—40 g DMS[a] powder daily
Length of Study:	6 mo
Approach:	Clinical biochemical battery physical examinations reporting and appearance of clinical reactions.

[a]Dried skim milk.

TABLE XV

Design of a Two-Month Acceptability Study with a Soy Protein Isolate (Supro 710)

Design	
Subjects:	100 adult subjects (50 experimental, 50 control)
Diets:	Experimental—40 g soy isolate daily
	Control—40 g DSM[a] powder daily
Length of Study:	2 mo
Approach:	Clinical biochemical battery Physical examinations Reporting and Appearance of clinical reactions

[a]Dried skim milk.

Long Term Tolerance and Acceptability of Soy Protein Products

Even though soy protein is frequently used as a milk substitute for infants allergic to formulas based on cow's milk, soy can also be a primary cause of allergy (60,61). Among atopic children, 5% had specific intracutaneous reactivity to soy, while 64% had a positive reaction to two or more members of the legume family, most often peanuts, string beans, lima beans, and green beans. Processing of protein foods is known to be capable of producing allergenic substances not detectable in the original product (62,63). Thus, although allergic reactions are uncommon with traditionally processed soy-containing foods compared with many other common foods of animal and plant origin, the possible effects of new processing procedures should always be taken into account.

A comprehensive evaluation of the role of soybean human protein nutrition must now include studies on the acceptability of, and tolerance to, the long term ingestion of the soy protein products that represent forms of preparation not previously experienced by man, or at levels of intake higher than those on which human experience has been accumulated. These studies must be conducted under close medical supervision and supported by appropriate laboratory procedures.

We have conducted two such acceptability studies at MIT. In the first study (Table XIV), a total of 40 healthy adult subjects were selected and randomized into two groups; one consisted of nine men and nine women consuming daily 40 g of Soy Protein Isolate 620; the other a double-blind group of eleven men and eleven women who consumed an equivalent amount of skim milk powder. The soy and milk powder were incorporated into fruit juices, and were consumed in addition to the free-choice diets of the subjects. One subject in the experimental group, a 21-year-old woman, developed mild gastrointestinal symptoms, nausea, and diarrhea approximately two hours after comsuming the material. Follow-up tests suggested that the symptoms in this subject were associated with the ingestion of Soy Protein 620 and commercial products containing it, but not with soy curd or TVP from another manufacturer. The reaction was mild and, with repeated testing, the sensitivity gradually disappeared before a specific cause could be identified.

The remaining subjects of both groups completed the study uneventfully, without any adverse reaction of any kind that could be attributed to the ingestion of the test product. Blood samples were drawn initially and at 60 and 180 days of the study for an extensive battery of biochemical analyses. The experimental group showed no changes or differences of clinical significance relative to those in the control group.

A second study was conducted on the acceptability of and tolerance to Soy Protein 710. This study was carried out in a larger sample of subjects, as shown in Table XV. All of the subjects completed the study uneventfully and without significant complaints. Gastrointestinal function remained normal throughout the study, and no nausea, abdominal discomfort, loose stools, constipation, or increased gas were reported. No allergic responses were observed, nor were there any changes in blood chemistries in the experimental group compared with those of the control group.

Kies and Fox (39) monitored blood components of subjects consuming various textured soy protein products. All values for all subjects remained within the normal range during the experimental diet periods. Bressani et al. (52) showed, in their studies with children consuming another texturized food from soybean protein isolate, that the test product was readily accepted by all. There were no adverse effects noted at any time during the experiment. Good acceptability of and tolerance to soy protein-based formulas in the newborn are also apparent from the extensive studies by Foman and coworkers (14).

Most reports of nutritional studies with soy protein products in humans make no specific mention of the acceptability of or tolerance to the material tested. If significant problems of intolerance had occured, however, it is likely that they would have at least been noted. We conclude that well processed soy products consumed over long periods of time are well tolerated and accepted by human subjects.

ACKNOWLEDGMENTS

We thank Allan Wayler, Eduardo Queiroz and Myriam Puig, and Edwina Murray for their key roles in the conduct of the unpublished M.I.T. studies. The financial support given by the Ralston-Purina Company, St. Louis, MO, and the help and advice of C. Hardin, D. Hopkins, and R. Steinke are greatly appreciated. We are most grateful to S. Fomon and his colleagues for allowing us to read their manuscripts and to discuss their results before they have been published. Also, we appreciate the privilege extended to us by C. Inoue and his coworkers in sharing their data with us prior to preparation for detailed publication. Our M.I.T. studies utilized the facilities of the M.I.T. Clinical Research Center, supported by a grant (RR-88) from the Division of Research Resources, National Institutes of Health.

REFERENCES

1. Young, V.R., and N.S. Scrimshaw, in Proceedings of the International Soya Protein Food Conference, Am. Soybean Assoc. Hudson, IA, 1978, pp. 18-29.
2. Scrimshaw, N.S., and V.R. Young, in "Keystone Conference – Soy Protein and Human Nutrition," Edited by H.L. Hilcke, D.T. Hopkins, and D.H. Waggle, New York Academic Press, NY (In press), 1978.
3. Handy, D.M., JAOCS 51:85A (1974).
4. Bressani, R., Ibid. 52:254A (1975).
5. Bressani, R., in Proceedings of the Internaional Soya Protein Food Conference, Am. Soybean Assoc., Hudson, IA, 1978, pp. 30-34.
6. Keystone Conference – Soy Protein and Human Nutrition, Edited by H.L. Wilcke, D.T. Hopkins, and D.H. Waggle, Academic Press, NY, (In press), 1978.
7. FAO/WHO, "Energy and Protein Requirements," FAO Nutrition Meetings. Dept. Scr. No. 52. Food and Agriculture Organization of the United Nations, Rome, 1973.
8. National Academy of Sciences, "Improvement of Protein Nutriture," National Res. Council. Committee on Amino Acids, National Academy of Sciences, Washington, D.C., 1974.
9. Arroyave, G., in "Nutrients in Processed Foods Proteins," Edited by P.L. White and D.C. Fletcher, Publishing Sciences Group, Inc., Acton, MA, 1974, pp. 15-28.
10. Young, V.R., and N.S. Scrimshaw, in "Protein Resources and Technology: Status and Research Needs," Edited by M. Milner, N.S. Scrimshaw, and D.I.C. Wang, AVI Publ. Co., Inc., Westport, CT, 1978, pp. 136-173.
11. Scrimshaw, N.S., and V.R. Young, in "International Encyclopedia of Food and Nutrition," Vol. 11, Chpt. 11, Edited by E.J. Bigwood, Pergaman Press, Oxford, and New York, 1972, pp. 363-380.
12. Young, V.R., W.R. Rand, and N.S. Scrimshaw, Cereal Chem. 54:929 (1977).
13. Hegsted, D.M., in "Improvement of Protein Nutritive," National Research Council, Committee on Amino Acids, National Academy of Sciences, Washington, D.C., 1974.
14. Fomon, S.J., and E.E. Ziegler, in "Keystone Conference Soy Protein and Human Nutrition," Edited by H.L. Wilcke, D.T. Hopkins, and D.H. Waggle, Academic Press, NY (In press), 1978.
15. Jung, A.L., and S.L. Carr, Clin. Pediatr. 16:982 (1977).
16. Omens, W.B., W. Leuterer, and P. Gyorgy, J. Pediatr. 62:98 (1963).
17. Andrews, B.F., and L.N. Cook, Am. J. Clin. Nutr. 22:845 (1969).
18. Fomon, S.J., Pediatrics. 24:577 (1959).
19. Dean, M.E., Med. J. Austr. 1:1289 (1973).
20. Cherry, F.F., M.D. Cooper, A.D. Stewart, R.V. Platou, Am. J. Dis. Child. 115:677.
21. Bates, R.D., W.W. Barreti, D.W. Anderson, and S.S. Saperstein, Annals of Allergy 26:577 (1968).
22. Cowan, C.C., R.C. Brownlee, W.R. De Looche, H.P. Jackson, and J.P. Matthews, Jr., S. Med. J. 62:389 (1969).
23. Fomon, S.J., L.N. Thomas, L.J. Filer, Jr., E.E. Ziegler, and M.T. Leonard, Acta Paed. Scand. Suppl. 223 (1971).
24. Fomon, S.J., L.N. Thomas, L.J. Filer, Jr., T.A. Anderson, and K.E. Bergmann, Ibid. 62:33 (1973).
25. Graham, G.G., R.P. Placko, E. Morales, G. Acevedo, and A. Cordano, (1970).
26. Dutra de Oliveria, J.E., L. Scantena, Netto N de Oliveira and G.G. Duarte, J. Pediatr. 69:670 (1966).
27. Torun, B., and F. Viteri, (1978). "Soy and Soybean Products for Human Consumption," XIth Intl. Congress Nutr. Rio de Janeiro, Brazil, Aug. 27-Sept. 1, 1978.
28. DeMaeyer, E.M., and H. Vanderborght, J. Nutr. 65:335 (1958).
29. Carroll, K.K., Nutr. Rev. 36:1 (1978).
30. Carroll, K.K., P.M. Giovannetti, M.W. Huff, O. Moase, D.C.K. Roberts, and B.M. Wolfe, Am. J. Clin. Nutr. 31:1312 (1978).
31. Graham, G.G., in "Amino Acid Fortification of Protein Foods," Edited by N.S. Scrimshaw and A.M. Altschul, M.I.T. Press, Cambridge, MA, 1971, pp. 222-236.
32. Korslund, M., C. Kies, and H.M. Fox, J. Food Sci. 38:637 (1973).
33. Kies, C., and H.M. Fox, Ibid. 36:841 (1971).
34. Zezulka, A.Y., and D.H. Calloway, J. Nutr. 106:121 (1976).
35. Zezulka, A.Y., and D.H. Calloway, Ibid. 106:1286 (1976).
36. Boggs, R.W., J.T. Rotruck, and R.A. Damico, J. Nutr. 105:326 (1975).
37. Rotruck, J.T., and R.W. Boggs, J. Nutr. 105:331 (1977).
38. Rotruck, J.T., and R.W. Boggs, Ibid. 107:357 (1977).
39. Kies, C., and H.M. Fox, J. Food Sci. 38:1211 (1973).
40. Bressani, R., N.S. Scrimshaw, M. Behar, F. Viteri, J. Nutr. 66:501 (1958).
41. Scrimshaw, N.S., R. Bressani, M. Behar, and F. Viteri, J. Nutr. 66:485 (1958).
42. Bressani, R., D.L. Wilson, M. Behar, and N.S. Scrimshaw, J. Nutr. 70:176 (1960).
43. "Recommended Dietary Allowances," 8th Edition, Food and Nutrition Board, National Academy of Sciences, 1974.
44. Fomon, S.J., E.E. Ziegler, L.J. Filer, S.E. Nelson, and B.B. Edwards, (Submitted for publication).
45. Fomon, S.J., Pediatrics 56:350 (1975).
46. Rama Rao, P.B., H.W. Norton, and B.C. Johnson, J. Nutr. 73:38 (1961).
47. Said, A.K., and D.M. Hegsted, Ibid. 100:1363 (1970).
48. Chen, C.F., H. Wei, P.C. Huang, and T.C. Tung, in "Progress in Meeting Protein Needs of Infants and Preschool children," Public 843, National Academy of Sciences – National Research Council, Washington, D.C., 1961, pp. 247-250.
49. Dutra de Oliveira, J.E., N. de Souza, T.A. de Rezende, L.R. Velente, V.F. Boyd, and E.E. Daggy, J. Food Sci. 32:131 (1967).
50. Dutra de Oliveira, J.E., and N. deSouza, Arch. Latinoamer Nutr. 17:197 (1967).

51. Bressani, R., F. Viteri, D. Wilson, and J. Alvarado, Arch Latinoamer. Nutr. 22:227 (1972).
52. Bressani, R., F. Viteri, L.G. Elias, S. de Zaghi, J. Alvarado, and A.D. O'Dell, J. Nutr. 93:349 (1967).
53. Viteri, F., C. Martinez, and R. Bressani, in "Mejoramiento Nutricional de Maiz," Edited by R. Bressani, J.E. Braham, and M. Behar, INCAP. Publication L-3, Institute of Nutrition of Central America and Panama, Guatemala, (1972), pp. 195-208.
54. Graham, G.G., E. Morales, G. Acevedo, R.P. Placko, and A. Cordano, Am. J. Clin. Nutr. 24:416 (1971).
55. Graham, G.G., J.M. Baertl, R.P. Placko, and A. Cordano, Ibid. 25:875 (1972).
56. Horan, F., in "New Protein Foods," Vol. 1A, Technology, Chpt. 8, Edited by A.M. Altschul, Academic Press, NY, (1974).
57. Tannenbaum, S.F., in "Nutrition and Agricultural Development," Chpt. 40, Edited by N.S. Scrimshaw and M. Behar, Plenum Press, NY, (1976).
58. Young, V.R., L. Fajardo, E. Murray, W.M. Rand, and N.S. Scrimshaw, J. Nutr. 105:534 (1975).
59. Inoue, G., T. Takahashi, K. Kishi, and T. Komatsu, "Soy and Soybean Products for Human Consumption," XIth Internaional Congress Nutrition, Rio de Janeiro, Brazil, Aug. 27 – Sept. 1, 1978.
60. Fries, J.H., J. Asthma Res. 3:209 (1966).
61. Fries, J.H., Ann. Allergy 29:1 (1971).
62. Scrimshaw, N.S., in "Single-Cell Protein II," Edited by S.R. Tannenbaum and D.I.C. Wang, M.I.T. Press, Cambridge, 1975, pp. 24-25.
63. Scrimshaw, N.S., and J.C. Dillon, in "Investigations on Single-Cell Protein," Edited by N.S. Scrimshaw, Pergamon Press, NY (In press).