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9. ABSTRACT

The protein of CSM, a cornmeal-soy flour-milk solids mixture now being used extensively in child feeding, has been demonstrated to have a biological value approximately two-thirds of that of casein. To be the main source of protein in the diet it should provide 12% of total calories as protein. Its digestibility is relatively poor, as is that of most vegetable mixtures. Its biological value might be enhanced by methionine enrichment or by improving its digestibility.

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Subject: Progress Report on CSM
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New Protein Sources for the Prevention
of Malnutrition.

For many years milk solids have been the mainstay of emergency child feeding programs throughout the world; their success has been varied. Possible limitations in the available supply and the real nature of the rejection and the untoward reactions encountered in many programs have directed our attention to other sources of supplementary protein. The untoward reactions, mainly diarrhea, were for a long time attributed to poor hygiene and ignorance; we now suspect that most of them were probably due to the lactose intolerance after weaning which is the rule, rather than the exception, in many parts of the world (1).

Approximately three years ago a cornmeal-soy-milk mixture (CSM) was introduced in many child feeding programs as an alternative to milk solids. Its acceptability and tolerance are already well established. The present report covers our evaluation of its protein quality in infants and children.

MATERIALS

CSM is a blend of 68% gelatinized processed cornmeal, 25% toasted defatted soy flour, and 5% regular nonfat dry milk plus mineral and vitamin mixtures. One hundred grams contain 19.0 g protein, 2.0 g fat and 65.6 g carbohydrate, and yield 347 kcal.

The modified milk (M) used in some of these studies was Similac with Iron[1].

The casein used was Casec[2].

Cornstarch, cane sugar and cottonseed oil were used when necessary to complete the diets.

"Complete" vitamin and mineral mixtures (2) were routinely added to the diets.

METHODS

Comparisons with milk protein at critical levels of intake (6.4 to 7.3% protein calories in an otherwise adequate diet), prolonged feeding (6.4 to 8.0% protein calories), and determinations of the supplementary effect of methionine (at 6.4 and 6.6% protein calories) were carried out in convalescent infants and children who had originally been admitted to the British American Hospital with severe malnutrition and diarrhea. Details of diet calculation and preparation and of the methods used for serum albumin and nitrogen determinations have already been reported (2). The technique for plasma amino acids and the rationale for the values used in reporting these have also been reported (3). CSM was also used in the initial dietary management of two infants with severe marasmus, at levels which were individually adjusted. It was not used in the initial management of kwashiorkor because of the unfavorable trend in serum albumin levels seen in these two children, something we have already encountered with other sources of protein (4).

RESULTS

Table I summarizes the comparative studies. At the beginning of these the first child had, at age 22 months, a "height age" of 12 months and a "weight age" of 8 months, based on a well-known U. S. standard (5). His serum albumin was a high normal 4.53 g/100 ml after 81 days in the hospital. During the initial 15 days on modified

milk, nitrogen (N) absorption was only 66% of intake and retention a low (for milk protein) 16% of intake. There was a significant drop in serum albumin, probably the result of rapid weight gain in the face of poor absorption and retention of N at a critical level of protein intake. Early in the CSM period N absorption and retention were quite poor but weight gain continued and serum albumin fell significantly. In the second half of the period N absorption improved notably and so did retention, with some recovery of serum albumin. The final period on casein revealed markedly improved retention of N, continued weight gain and recovery of serum albumin.

In the second child (#160M), considerably younger than the first, absorptions and retentions of N from CSM were consistently satisfactory, almost identical to those from casein. Weight gain was at an accelerated rate and serum albumin, though falling slightly, remained at high normal levels. In the third child (#209M) the retention of N from CSM was approximately 65% of that from casein, weight gains were of approximately equal magnitude, and serum albumin was stable. In the remaining three cases the results were similar, with the exception of a striking fall in the serum albumin of #225M. This was associated with the presence of occult blood in the stools during most of this period.

During prolonged feeding (Table II) at varying levels (6.4 to 8.0% calories) in two children, the increments in height and weight ages equalled or exceeded those in chronologic age. In other words,

CSM supported a significantly accelerated rate of growth, in every respect similar to that expected from milk-based diets in convalescent malnourished infants in our unit (6).

The results in the initial management of two marasmic infants (Table III) were generally unsatisfactory. In the first child the early sharp drop in serum albumin level was not surprising, as it is a common consequence of rapid expansion of extracellular fluid volume. This child had a heavy burden of infections on admission and then proceeded to develop varicella. From the 44th to the 51st days, despite excellent nitrogen retention, his weight gain was so rapid as to suggest an abnormal expansion of extracellular fluid. This was confirmed by a marked drop in serum albumin and the appearance of visible edema. An immediate change to a milk diet resulted in prompt diuresis and reversal of the fall in serum albumin, despite N retentions that were not strikingly higher.

In the second child, at more favorable protein to calorie ratios, retentions of N were affected by variations in absorption but were generally satisfactory. An initial brusque fall in serum albumin was partially but not completely reversed until milk was given. In this case an episode of varicella also affected the results.

In two convalescent children (Table IV) the possible supplementary effect of methionine was studied. In the first of these, age 27 months, there was no apparent benefit from the addition to the diet of 10 mg of DL-methionine/kg body wt/day. In the second, only 15 months of age, there was a demonstrable improvement in the amount of N retained,

the rate of weight gain, and in serum albumin levels.

In Table V we have reported in an abbreviated form the results of the fasting plasma free amino acids of eleven children who had been receiving CSM as their only source of dietary protein for varying periods of time. In the first three children, whose plasma was obtained at the end of relatively short comparative studies, "total" and "essential" amino acids were considerably lower than those previously reported for similar levels of protein intake from milk or wheat proteins (3). The ratio of plasma essential to total amino acids (EAA/AA) was very similar to that of our wheat diets, both being generally inferior to those of the milk diets. The molar fraction of methionine, the presumed first-limiting amino acid, was quite variable.

Total and essential amino acids in plasma from the methionine supplementation study (#219) were higher than in the three previous children, despite equivalent intakes. This may be a function of the considerably better absorption rates: 76 and 81% as against 77, 70 and 63% of intake. The essential to total ratios were moderately higher than in the previous cases, and there was a suggestive elevation in the molar fraction of methionine after supplementation.

After prolonged feeding total and essential amino acid levels were low, particularly in #157, whose intake was lower and who in previous comparative studies (Table I) had demonstrated relatively poor absorption rates: 57 and 74% of nitrogen intake. Despite

this the EAA/AA ratio was similar to that of milk protein diets. The other child, #169 , had a very low ratio but nevertheless was growing satisfactorily at the time.

The samples obtained during the initial management of #209 were suggestive of dietary protein inadequacy and he was indeed not progressing satisfactorily. Those from #213, with a significantly higher intake and a more satisfactory course, were more like those of milk diets, particularly the first of the two samples.

When the mean values are compared to those of milk diets, it is again evident that total and essential amino acids are lower, as is their ratio. If the two last values, from a child on a higher protein intake, are excluded the differences would be more impressive. There was no distinct trend in the molar fraction of methionine.

DISCUSSION

When vegetable proteins or mixtures of these are used in infant and child feeding it is generally recognized that because of their lower content of total essential amino acids, their low content of certain individual essential amino acids, and their usually inferior digestibility, they will almost certainly have an inferior biological value and that this must be compensated for by increasing the protein intake of the diet. This, however, does not necessarily guarantee equivalent rates of growth (7). It must also be recorgnized that very high protein intakes result in higher renal solute loads and the concommitant risk of dehydration (8). Consequently, the necessary

increase in protein intake must be of a reasonable magnitude, preferably within the limits of that generally considered safe in infants drinking whole cow's milk yielding approximately 15% of calories as protein, approximately double the intake of the breast fed infant. A dietary protein with a biological value approximately 65% of that of milk protein and consequently requiring a 50% increase in the protein content of the diet, to 12% of total calories, would presumably fall within this safe range, assuming of course that equivalent growth rates were attained.

In short-term studies comparative rates of apparent N retention are our most reliable index of biological value (9). Examination of the results in Table I reveals that for the six children studied N retention from CSM was 65, 98, 64, 80, 62 and 50% of that from milk protein (almost invariably casein) in dietary periods immediately preceding and following the CSM periods. The fact that the studies were carried out at levels of protein intake which were on the border of adequacy suggests that these figures are a fairly accurate representation of relative biological values. The studies of prolonged feeding are confirmatory.

The average rate of apparent N absorption from the milk protein was 83% of intake, while that from CSM was only 70% of intake, a typical figure for most of the intact vegetable products we have studied, with the notable exception of white wheat flour (3) and soy milks made from isolated soy protein (unpublished data). That this in itself accounts for much of the difference in biological

value is suggested by the apparent correlation between absorption rates and plasma amino acid concentrations. The episode of silent blood loss in one case may well have been accompanied by loss of serum proteins into the gut. We have seen a similar episode in one other child on a completely different diet.

Methionine is clearly the first-limiting amino acid in all intact soy proteins and this can be easily demonstrated in the human infant (10). In the CSM mixture the two major sources of protein, corn and soy, have different amino acid deficiencies and a true complementary effect is to be expected. Examination of the amino acid composition of the final mixture indicates that methionine is probably first-limiting, but not to the degree that it is in soy alone. Failure to demonstrate a supplementary effect of methionine in one of the two children could conceivably be explained on the basis of his more advanced age and presumably lower methionine requirement. The manifestly inferior nitrogen retentions and rates of weight gain, when compared with those of the casein periods, suggest that this is not the explanation. It is more likely that the significantly poorer rates of N absorption, 72 and 66% of intake from CSM as against 88, 84 and 80% of intake from casein, made total nitrogen first-limiting. In the second case the supplementary effect was clear-cut.

Failure to support satisfactory "initiation of cure" in the severely malnourished is the rule rather than the exception with proteins other than those of milk (4). There are many possible

explanations not within the scope of this report: CSM was no better and no worse in this respect than other vegetable protein mixtures.

Although there was enough variability in the plasma amino acid values to make reliance on a single determination hazardous, there were distinct trends apparent. These results, combined with those from our milk protein and wheat studies (3), suggest that the determination of total fasting plasma free amino acids might well be used to measure indirectly the efficacy of intestinal digestion and absorption of dietary protein, assuming a relatively steady state and making comparisons with a standard protein at isonitrogenous levels of intake. The interpretation of essential to total amino acid ratios is more complex. That these reflect the same ratios in the dietary protein is undoubtedly true, at least at the low levels of intake used in our studies. At the same time, however, this ratio is affected by the adequacy of a particular protein intake for a given calorie intake and rate of growth, as demonstrated by Snyderman et al (11). In this study the molar fraction of the presumed first-limiting amino acid, methionine, did not prove as sensitive as that of lysine in our wheat studies (3). If it were not in reality first-limiting, or only for some of the children due to variability in absorption and in requirements, or if its plasma level were not as sensitive to marginal deficiency, this failure might be explained.

These studies indicate that CSM can be the main source of protein in the diet of rapidly growing infants and children. Its biological value is approximately 60 to 65% of that of casein. If it is to be the nearly exclusive source of protein in the diet, its

protein should provide no less than 12% of total calories, assuming 8% of calories to be a safe level when casein is the dietary protein. Since the product has approximately 22% of calories as protein there is considerable room for dilution with non-protein calories. Experience tells us, however, that more than 100% dilution could and does occur in practice and that it would be desirable to increase the margin of safety. To do so by merely increasing the protein content would expose many children to the hazards of an excessive solute load. A more desirable alternative is that of increasing the biological value. That this might be done with methionine enrichment, a simple expedient, is suggested by our results: these observations should be confirmed or expanded. A second or simultaneous step would be to improve the digestibility of the product: this might be accomplished through the use of a different source of soy protein. Sick or malnourished children should be given cow's milk derivatives or their nutritional equivalent.

SUMMARY

The protein of CSM, a cornmeal-soy flour-milk solids mixture now being used extensively in child feeding, has been demonstrated to have a biological value approximately two thirds of that of casein. To be the main source of protein in the diet it should provide 12% of total calories as protein. Its digestibility is relatively poor, as is that of most vegetable mixtures. Its biological value might be enhanced by methionine enrichment or by improving its digestibility.

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FOOTNOTES

[1] Kindly supplied by Ross Laboratories, Columbus, Ohio.

[2] Kindly supplied by Mead Johnson International, Evansville, Ind.

TABLE I

Evaluation of CSM as sole source of protein in diet of six convalescent malnourished infants. Comparisons with modified cow's milk (M) and casein (C) by nitrogen balance, rate of weight gain (Δ wt), and changes in serum albumin.

Protein		No.		Nitrogen balances				Δ wt	Ser. albumin	
Source	% of Kcal	of days	On days	mg/kg/day int.	mg/kg/day ret.	% of int. abs.	% of int. ret.	g/kg /day	g/100 ml Δ	g/100 ml Final
#157M - Hosp. day 81 - Age 22 mo. - 75 cm (12 mo) - 8.67 kg (8 mo)										
M	6.4	15	7-15	320	50	66	16	4.3	-0.51	4.02
CSM	6.4	30	1-9	311	23	57	8			
			25-30	321	97	74	30	2.1	-0.44	3.58
C	6.4	36	1-6	320	119	78	37			
			9-20	315	131	79	42	2.8	0.50	4.08
#160M - Hosp. day 54 - Age 8 mo. - 63 cm (4 mo) - 5.55 kg (3 mo)										
C	6.7	12	6-11	400	147	84	37	8.2	0.75	4.68
CSM	7.3	30	2-10	432	115	73	27			
			11-22	429	132	80	31			
			28-30	440	150	76	34	3.7	-0.39	4.29
C	6.7	40	1-6	390	85	78	22			
			34-40	384	112	78	30	3.9	0.07	4.36
#209M - Hosp. day 86 - Age 33 mo. - 75.5 cm (13 mo) - 8.20 kg (7 mo)										
C	6.4	9	4-9	320	91	91	28	6.3	-0.19	4.26
CSM	6.4	15	7-15	320	60	77	19	5.5	-0.03	4.23
C	6.4	9	4-9	320	95	88	29	4.9	-0.11	4.12
#225M - Hosp. day 112 - Age 11 mo.- 61.5 cm (3½ mo) - 4.82 kg (1½ mo)										
C	6.7	9	4-9	400	157	82	39	10.1	0.32	3.95
CSM	6.7	12	4-12	400	130	70	32	4.6	-1.00	2.95*
C	6.7	9	4-9	400	167	82	42	5.1	0.42	3.37
#227 M - Hosp. day 116 - age 11 mo. - 63.5 cm (4½ mo) - 6.93 kg (5 mo)										
C	6.4	9	4-9	320	131	87	41	7.3	-0.62	4.06
CSM	6.4	9	4-9	320	90	63	28	4.8	-0.24	3.82
C	6.4	9	4-9	320	157	88	49	2.9	-0.07	3.75
#234M - Hosp. day 40 - age 22 mo. - 75.6 cm (13 mo) - 7.68 kg (8 mo)										
C	6.4	9	4-9	320	115	87	36	6.8	-0.07	4.13
CSM	6.4	12	4-12	320	59	72	19	3.8		
C	6.4	9	4-9	320	130	88	40	3.9		4.15

* Possible transient protein-losing enteropathy.

TABLE II

Prolonged feeding of CSM as the sole source of protein in the diet of two convalescent malnourished infants. Evolution of chronologic age (CA), height age (HA), weight age (WA), and serum albumin (SA).

Case and Sex	No. of Days	Initial (in months)			Advance (in months)			Serum albumin g/100 ml	
		CA	HA	WA	CA	HA	WA	Δ	Final
157M	49[1]	26	15	12	1.6	3.0	3.0	0.27	4.59
169M	159[2]	14	5	6	5.3	5.0	7.2	-0.28	4.01

[1] #157M received 100 Kcal (8.0% protein) /kg/day for 35 days, and 125 Kcal (6.4% prot.) /kg/day for 14 days.

[2] #169M received (per kg/day) 150 Kcal (6.7% prot.) for 22 days, 125 Kcal (6.4% prot.) for 65 days, and 125 Kcal (8.0% prot.) for 72 days.

TABLE III

CSM in the initial dietary management of two marasmic infants [1].

DIET					N BALANCES				Δ wt	Ser.albumin	
Protein &		Kcal/kg/day		No.	On	mg/kg/day		%	g/kg	g/100 ml	
g/kg/day		& % prot.		days	days	int.	ret.	abs.	/day	Δ	Final
#209M - 30 months - 74 cm (11.5 mo) - 6.64 kg (5 mo)											
CSM	1.0	50	8.0	2	-	-	-	-	10.0	-0.51	4.30
	2.0	100	8.0	12	-	-	-	-	2.6	-0.66	3.64
	2.5	150	6.7	24	-	-	-	-	3.1	-1.35	2.29
	1.25	75	6.7	6	4-6	200	-20	51	-1.8	0.51	2.80
	2.5	150	6.7	7	1-6	400	153	79	14.4	-0.82	1.98
MILK	2.5	150	6.7	6	1-6	400	178	71	-5.5	1.00	2.98
#213M - 9 months - 62.1 cm (4 mo) - 5.09 kg (2 mo)											
CSM	2.2	88	10.0	8	-	-	-	-	-8.2	-0.23	3.71
	2.5	125	8.0	16	10-16	400	69	72	6.2	-1.16	2.55
	3.0	125	9.6	22	1-6	480	158	80	0.1	0.95	3.50
	3.0	150	8.0	26	5-10	480	48	56			
					12-17	480	133	68			
					23-26	480	174	74	7.1	-0.45	3.05
MILK	3.0	150	8.0	12	1-9	480	179	81	1.4	0.54	3.59

[1] On admission #209 had a urinary tract infection, a progressive BCG vaccination, ascaris infestation and severe anemia requiring transfusion. He developed varicella during the third hospital week and became edematous on the 49th day. #213 developed varicella during the third week and edema a few days later.

TABLE IV

DL-methionine supplementation of CSM fed at critical levels as the sole source of protein in the diet of two convalescent malnourished infants. Comparisons with casein (C) in consecutive diet periods.

AGE in mo.	DIET				N BALANCES mg N/kg/day		Δ wt g/kg /day	Ser. albumin g/100 ml	
	Protein	% of Kcal	DL-met. /kg/day	No. days	in.	ret.		Δ	Final
27	C	6.6	-	10	264	98	2.7	-0.25	4.30
	CSM	6.6	-	15	257	59	1.8	-0.19	4.11
	C	6.6	-	9	264	113	2.9	-0.14	3.97
	CSM	6.6	10 mg	15	262	64	1.9	-0.35	3.62
	C	6.6	-	9	264	89	-	0.32	3.94
15	C	6.4	-	9	320	102	3.2	0.19	3.87
	CSM	6.4	-	15	320	82	2.6	-0.18	3.69
	C	6.4	-	9	320	112	3.9	0.01	3.70
	CSM	6.4	12 mg	15	320	114	5.0	0.21	3.91
	C	6.4	-	9	320	124	3.2	0.73	4.64

TABLE V

Fasting plasma free amino acids of infants receiving CSM as the sole source of dietary protein. Total amino acids (AA), total essential amino acids (EAA), the ratio of essentials to total (EAA/AA), and methionine as the molar fraction of essentials (met/EAA). Control values are from 39 infants receiving milk protein as 6.4 - 8.0% of calories

Case No.	Protein g/kg /day	Protein % of kcal	No. of days This diet	No. of days On CSM	Plasma Amino Acids AA µM/ml	Plasma Amino Acids EAA µM/ml	Plasma Amino Acids EAA/AA	Plasma Amino Acids met/EAA
During comparative studies (Table I)								
209	2.0	6.4	15	15	1.851	0.434	0.234	0.057
225	2.5	6.7	9	9	1.685	0.397	0.236	0.030
227	2.0	6.4	9	9	1.632	0.427	0.262	0.021
During supplementation studies (Table IV)								
219	2.0	6.4	15	15	1.914	0.561	0.293	0.041
219[1]	2.0	6.4	15	15	2.373	0.601	0.253	0.060
After prolonged feeding (Table II)								
157	2.0	6.4	14	49	1.338	0.423	0.316	0.035
169	2.5	8.0	72	159	1.679	0.305	0.182	0.056
During initial dietary management (Table III)								
209	2.5	6.7	7	21	1.679	0.315	0.188	0.035
209	2.5	6.7	7	51	1.719	0.293	0.170	0.058
213	3.0	8.0	17	63	2.726	0.944	0.346	0.039
213	3.0	8.0	25	71	2.649	0.615	0.232	0.031
MEAN FOR CSM DIETS					1.931	0.483	0.247	0.042
S. D.					0.450	0.190	0.057	0.013
MEAN FOR CONTROLS					2.298	0.691	0.296	0.032
S. D.					0.192	0.086	0.024	0.006

[1] DL-methionine, 12 mg/kg/day, added to diet.