Lactose-Free, Medium-Chain Triglyceride Formulas in Severe Malnutrition

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A lactose-free, medium-chain triglyceride (MCT)–casein formula (Lactose-Free Portagen) was used with success in the management of four children with kwashiorkor and three infants with persistent hypoalbuminemia, two of whom had associated infections. A second formula (Pregestimil), based on a casein hydrolysate and MCTs, with dextrose as the major carbohydrate, was used successfully in five infants with severe marasmus, one with kwashiorkor, and five with marasmus, severe diarrhea, and infection. The absence of lactose was of definite benefit, as was probably the MCT content. It is probable that the dextrose was of benefit to some of the sickest infants but this was not proved in these studies.

Transient lactase deficiency is a common complication of severe infantile diarrhea. In more prolonged cases other disaccharidases may be affected, and in the extreme, monosaccharide absorption can be impaired.[1] In severe malnutrition, flattening and dystrophy of the intestinal mucosa cause a relative decrease both in absorptive surface and in disaccharidase activity, particularly of lactase, leading to a limited tolerance for lactose. After the first year of life, genetically determined decreases in lactase activity may already be present or may be precipitated prematurely by the malnutrition, with consequent failure to recover maximal lactose tolerance during convalescence.[2]

Where severe malnutrition is prevalent, milk must be used cautiously in initial management. In the United States it is common practice during recovery from severe diarrhea to use lactose-free protein hydrolysates or soy protein formulas, either routinely or after failure with lactose-containing formulas.

Some degree of fat malabsorption is evident in severe diarrhea and may aggravate it[3]; it is well documented in malnutrition.[4] When dietary fat is curtailed for this reason, calorie density is decreased, weight gain is delayed, and convalescence prolonged. In some situations, particularly after extensive intestinal resection, fat malabsorption is of serious import; in such situations medium-chain triglycerides (MCT) are of value in assuring an adequate energy supply.[5]

Although total intravenous alimentation has found increasing use in the management of diarrhea and malabsorption, it is not always an innocuous procedure[6] and at times is used without trying simpler alternatives. The availability of MCT-containing formulas, without lactose or with no disaccharides at all, broadens the possible choices and should increase the percentage of complex cases manageable by the oral route.

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Rheumatic fever prevention.
Here's true convenience for patients who must receive prophylactic penicillin indefinitely. A prolonged-action penicillin—benzathine penicillin G. Recommended as the method of choice* to prevent streptococcal infection and possible recurrence of rheumatic fever. A single monthly injection (1,200,000 units) offers continuous prophylaxis in most patients.

Action against strep.
In therapy of mild to moderate group A streptococcal pharyngitis (without bacteremia), prolonged action again commends this penicillin, named by authorities a method of choice.* Just one injection (600,000 to 900,000 units in children and 1,200,000 units in adults) usually maintains serum concentrations for the ten days considered necessary to eradicate the streptococci and preclude the initial onset of rheumatic fever.†

*Rheumatic Fever Committee of the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association.

Indications: In treatment of infections due to penicillin G-sensitive microorganisms susceptible to the low and very prolonged serum levels common to this dosage form. Therapy should be guided by bacteriological studies (including sensitivity tests) and clinical response.

The following infections usually respond to adequate dosage of IM benzathine penicillin G.

Streptococcal infections (Group A—without bacteremia). Mild to moderate upper respiratory infections (e.g., pharyngitis).

Venereal infections—Syphilis, yaws, bejel, and pinta.

Medical Conditions in which Benzathine Penicillin G Therapy is indicated as Prophylaxis:

Rheumatic fever and/or chorea—Prophylaxis with benzathine penicillin G has proven effective in preventing recurrence of these conditions. It has also been used as followup prophylactic therapy for rheumatic heart disease and acute glomerulonephritis.

FOR DEEP INTRAMUSCULAR INJECTION ONLY.

Contraindications: Previous hypersensitivity reaction to any penicillin.

Warnings: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported. Anaphylaxis is more frequent following parenteral therapy but has occurred with oral penicillins. These reactions are more apt to occur in individuals with history of sensitivity to multiple allergens. Severe hypersensitivity reactions with cephalosporins have been well documented in patients with history of penicillin hypersensitivity. Before penicillin therapy, carefully inquire into previous hypersensitivity to penicillins, cephalosporins and other allergens. If allergic reaction occurs, discontinue drug and treat with usual agents, e.g., pressor amines, antihistamines and corticosteroids.

Precautions: Use cautiously in individuals with histories of significant allergies and/or asthma.

Carefully avoid intravenous or intraarterial use or injection into or near major peripheral nerves or blood vessels, since such injection may produce neurovascular damage.

†In streptococcal infections, therapy must be sufficient to eliminate the organism, otherwise the sequelae of streptococcal disease may occur. Take cultures following completion of treatment to determine whether streptococci have been eradicated.

Prolonged use of antibiotics may promote overgrowth of nonsusceptible organisms including fungi. Take appropriate measures if superinfection occurs.

Adverse Reactions: Hypersensitivity reactions reported are skin eruptions (maculopapular to exfoliative dermatitis), urticaria and other serum sickness reactions, laryngeal edema and anaphylaxis. Fever and eosinophilia may frequently be only reaction observed. Hemolytic anemia, leucopenia, thrombocytopenia, neuropathy and nephropathy are infrequent and usually associated with high parenteral doses.

As with other antisyphilitics, Jarisch-Herxheimer reaction has been reported.

Composition: (units benzathine penicillin G as active ingredient): 300,000 units per cc.—10-cc. multi-dose vial. Each cc. also contains sodium citrate buffer, approximately 6 mg. lecithin, 3 mg. polyvinylpyrrolidone, 1 mg. carboxymethylcellulose, 0.5 mg. sorbitan monopalmitate, 0.5 mg. polyoxyethylene sorbitan monopalmitate, 0.14 mg. propylparaben and 1.2 mg. methylparaben.

600,000 units in 1-cc. TUBEX® (sterile cartridge-needle unit) Wyeth, packages of 10.

1,200,000 units in 2-cc. TUBEX, packages of 10, and in 2-cc. single-dose disposable syringe.

2,400,000 units in 4-cc. single-dose disposable syringe.

Each TUBEX or disposable syringe also contains sodium citrate buffer and, as w/v, approximately 0.5% lecithin, 0.4% carboxymethylcellulose, 0.4% polyvinylpyrrolidone, 0.01% propylparaben and 0.09% methylparaben.

Injection
BICILLIN® LONG-ACTING
(sterile benzathine penicillin G suspension)

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Month-long rheumatic fever prophylaxis gives freedom from daily dosage.

We have evaluated two such formulas in the management of complex nutritional problems.

Materials

Portagen.—Lactose-Free Portagen (3200-AH) is a lactose-free formula containing MCT as its major fat component and casein as its nitrogen source. On a dry basis it contains 16.4% protein (14% of calories); 22.7% fat (40% of calories), of which 19.7% is MCT oil (34.3% of calories), 2.6% corn oil (4.9% of calories), and 0.4% lecithin (0.8% of calories); 53.9% carbohydrate (46% of calories) of which 40.5% is maltodextrins (34.5% of calories), 13.3% sucrose (11.3% of calories), and less than 0.15% lactose (<0.13% of calories); 3.9% ash; and 3.4% moisture. When diluted to 0.68 kcal/ml, 1 liter contains 2,820 United States Pharmacopeia (USP) units vitamin A, 282 USP units vitamin D, 10 international units (IU) vitamin E, 53 mg ascorbic acid, 1 mg thiamine, 1.2 mg riboflavin, 12 mg niacinamide, 1.3 mg pyridoxine, 7 mg pantothenic acid, 3.3μg cyanocobalamin, 71μg folic acid, 35μg biotin, 95 mg choline, 95 mg inositol, 710 mg calcium, 560 mg phosphorus, 12 mg iron, 106μg iodine, 430 mg sodium, 1 gm potassium, 1 mg copper, 137 mg magnesium, 2 mg manganese, and 4 mg zinc.

Pregestimil.—Pregestimil (3200-AD) is a protein hydrolysate formula with MCT as the major fat component and dextrose as the major carbohydrate. It is made from 20% casein enzymatically hydrolyzed and charcoal treated, 17.4% MCT, 2.0% safflower oil, 17.9% arrowroot starch, and 39.7% dextrose. When diluted to 0.68 kcal/ml, 1 liter contains 1,590 USP units vitamin A, 420 USP units vitamin D, 5 IU vitamin E, 50 mg ascorbic acid, 0.46 mg thiamine, 1.8 mg riboflavin, 4 mg niacinamide, 0.5 mg pyridoxine, 3.2 mg Ca pantothenate, 4.5μg cyanocobalamin, 50μg folic acid, 30μg biotin, 160 mg choline chloride, 950 mg calcium, 690 mg phosphorus, 12 mg iron, 65μg iodine, 581 mg potassium, 0.4 mg copper, 50 mg magnesium, and 3 mg zinc.

Methods

All the infants studied were admitted to the British American Hospital in Lima, suffering from severe malnutrition, often complicated by acute diarrhea and dehydration, Gram-negative sepsis, and other infections. Nutritional support is urgent in most such children. Intravenous alimentation is used sparingly because conditions are not ideal and many patients are already infected. Prior to admission they have commonly received chloramphenicol, and in the hospital they are often given powerful antibiotic combinations for proved or suspected Gram-negative sepsis, making them extremely susceptible to superinfection with *Pseudomonas* or *Candida*. Peripheral veins are used freely for administration of electrolytes, dextrose, and amino acids but partial oral alimentation is attempted as soon as possible.

Techniques and methods used in the balance studies have been described previously, as have the vitamin and mineral mixtures used, either exclusively or to supplement those included in the products used.[7] Sodium, potassium, and magnesium intakes from oral feedings are usually maintained at 2.0, 3.3, and 0.5 mEq/kg of body weight per day, respectively, except in the initial management of the severely malnourished, when additional potassium and magnesium are usually necessary. When additional calories are added to the formulas, these are usually divided evenly between cottonseed oil and sucrose.

Results

Because of the known high biological value of the nitrogen source in both products, a limited number of studies were carried out to compare their utilization with that of our usual control mixture of casein, cottonseed oil, and sucrose. Infants 239 and 237, 5.2 and 13.5 months of age, respectively, well advanced in their recovery from malnutrition, received both formulas as the source of nitrogen, with preceding, intervening, and following casein periods. All periods were of nine days each, with nitrogen balance being determined during the last six days. Both received 100 kcal/kg/day, with 7.0% and 6.6% of calories as protein, recalculated daily. To achieve these critical percentages the formulas were diluted as indicated previously.

Stool dry weight, when estimated, was between 6.3 and 13.8 gm/day, with stool fat between 2.3 and 8.1 gm/day. Both were lower during administration of the two formulas than during administration of the control diet, but the number of observations was too small for statistical analysis. Apparent nitrogen absorption was 80% to 90% of intake from the control casein diets, 83% and 86% from Portagen, and 85% and 88% from Pregestimil. Apparent nitrogen retention was 30% to 34% of intake for the control diets, 34% and 37% for Portagen, and 29% and 34% for Pregestimil. None of the differences was significant when each test period was compared with the preceding and following control period. Calculated biological value, retention as a percentage of absorption, was similar for the three diets, although slightly higher for Portagen than for Pregestimil.

Rates of weight-gain in infant 239

Table 1.—Portagen Diet in Four Children With Kwashiorkor and Three With Persistent Hypoalbuminemia

Case, Sex	Age (mo)	Days Receiving Diet*	Serum Albumin Level: Initial (gm/100 ml)	Serum Albumin Level: Increase (gm/100 ml/day)	Edema Lost, Day
Kwashiorkor					
254, M	26.1	26	1.39	.095	12
255, M	23.7	33	1.03	.062	11
257, M	38.8	12	1.60	.035	12
262, M	23.3	18	1.50	.072	7
Persistent Hypoalbuminemia					
244, M	16.5	16	2.17	.123	none
246, F	6.5	35	2.18	.036	none
249, M	5.1	16	2.80	.101	none

* Diets, based on Portagen, provided 2.0 to 4.0 gm of protein and 75 to 150 kcal/kg of body weight per day.

were moderately higher, 3.3 and 4.1 gm/kg/day for Portagen and Pregestimil, respectively, than during the casein periods, when they were 2.4, 2.1, and 3.1 gm/kg/day. In infant 237 they were distinctly higher, 5.9 and 3.0 gm/kg/day for Portagen and Pregestimil and 0.5, 0.5, and 0.2 gm/kg/day during the casein periods. Although rates of weight gain during such short periods are not entirely reliable, they were inversely correlated with stool fat, and suggest that the MCT of the formulas were better utilized than the cottonseed oil.

In infant 242, 14.5 months of age, comparison was made only between Pregestimil and casein, with similar results for both.

Portagen was used in the initial management of four boys (infants 254, 255, 257, and 262) with uncomplicated marasmic kwashiorkor, 23.3 to 38.8 months old, an age at which malnutrition[2] or racial factors[8] can be expected to result in a high incidence of relatively low intestinal lactase activity. The results are summarized in Table 1.

All four children, as part of another study, received casein or modified milk during the first day of treatment. They were then given Portagen, diluted with sucrose and oil so that 8% to 10% of calories came from protein, in progressively increasing amounts. It was well tolerated, with no diarrhea; diuresis began in less than a week and was complete by the 12th day. Portagen was discontinued early because our supply was very limited. By this time steady weight gain had been established in all but infant 257.

Portagen was also used in the further management of three hypoalbuminemic infants (infants 244, 246, and 249) originally admitted with marasmus (Table 1).

Infant 244 had received a wheat-soy blend[9] as the source of protein for 51 days. Weight gain had been satisfactory for 36 days but then stopped despite an adequate intake and good

Table 2.—Pregestimil Diet in Four Infant Girls With Marasmus

Hospital Day	Daily Diet: Protein Source	Protein gm/kg	kcal/kg	Weight Change, gm/kg/Day	Serum Albumin Level, gm/100 ml; Final
	Infant 328—12.5 mo, 70.5 cm, 6.1 kg				
1-2	IV* fluids + amino acids			17.9	3.83
3-5†	Pregestimil	1.0	50	−17.1	2.91
6-11†	Pregestimil	1.6	50	18.9	3.12
12-13†	Pregestimil	2.0	75	−8.4	...
14-17	Pregestimil	2.5	100	−3.1	3.60
18-23	Pregestimil	3.0	125	13.2	...
24-34	Pregestimil	4.0	150	2.8	3.91
	Infant 346—8.1 mo, 63 cm, 4.4 kg				
1-4†	Pregestimil	1.4	70	29.0	3.63
5-11†	Pregestimil	2.5	125	−5.0	2.86
1[illegible]-14	Pregestimil	3.0	150	−0.7	...
15-16‡	IV fluids			−7.5	2.95
17-19†	Pregestimil	2.5	100	18.2	2.94
20-25†	Pregestimil	3.0	125	3.7	...
26-40	Pregestimil	4.0	150	7.5	3.74
	Infant 348—5.6 mo, 60.5 cm, 4.7 kg				
1-8†	Pregestimil	1.5	53	4.7	3.13
9-10§	IV fluids			1.0	...
11-13†	Pregestimil	0.9	33	−11.2	2.94
14-18	Pregestimil	2.2	85	−1.7	3.26
19-23	Pregestimil	3.0	125	9.6	3.43
	Infant 355—3.6 mo, 57.3 cm, 3.5 kg				
1	IV fluids			1.4	...
2-3†	Pregestimil	0.8	25	6.4	...
4-5	Pregestimil	1.6	50	−9.9	...
6-8	Pregestimil	2.0	75	1.0	...
9-10	Pregestimil	2.5	100	−1.4	3.61

* Intravenously administered.
† Plus IV fluids.
‡ Episode of circulatory collapse and *Pseudomonas* bacteremia.
§ Episode of bloody diarrhea.

Table 3.—Prolonged Pregestimil Diet in a 22.4-Month-Old Boy* With Marasmus (Infant 360)

Hospital Day	Daily Diet: Protein Source	Protein gm/kg	kcal/kg	Weight Change, gm/kg/Day	Serum Albumin Level, gm/100 ml	Observations
1	Casein	0.5	25	−24.2	3.66	Diarrhea; pneumonia
2-7	Pregestimil	1.8	67	6.3	...	...
8-13	Pregestimil	3.2	154	11.3	3.56	...
14-18	Pregestimil and milk	2.5	140	−3.0	3.73	...
19-41	Milk	2.5	150	2.5	3.41	Increasing stool weight and fat; diarrhea
42-43	Pregestimil	0.8	50	5.7	3.34	Giardiasis; flat LTT response
44-49	Pregestimil	2.0	125	2.5	3.99	...
50-62	Pregestimil	2.3	140	3.7	4.27	...
63-70	Casein	2.6	150	5.1	...	Diarrhea; pneumonia
71-75	Pregestimil	1.0	45	−7.3	3.71	Hypothermia; IV fluids
76-85	Pregestimil	2.9	118	5.8	4.27	...
86-98	Casein	2.0	125	2.0	4.29	Pneumonia
99-105	Pregestimil	3.0	125	4.4	...	...

* Admission length, 72 cm; weight, 6.25 kg. Last day of study length, 73.5 cm; weight, 8.68 kg.

Table 4.—Pregestimil Diet in Five Extremely Sick Malnourished Infants

Hospital Day	Daily Diet: Protein Source	Protein gm/kg	kcal/kg	Weight Change, gm/kg/Day	Serum Albumin Level, gm/100 ml	Observations
	Infant 359, M—8.8 mo, 63.5 cm, 4.4 kg					
1-4	IV fluids + amino acids			6.2	2.82	Diarrhea, acidosis, shock
5-8	Pregestimil	1.2	38	−4.0	2.59	Pneumonitis
9-11	Pregestimil	2.0	75	−3.0	2.73	...
12-21	Pregestimil	2.9	125	7.4	3.61	...
22-25	Pregestimil	4.0	175	10.8	3.50	...
	Infant 330, M—3.5 mo, 55.5 cm, 3.15 kg					
1-7	Pregestimil	1.2	60	−2.7	3.52	Diarrhea, scabies
8-10	Pregestimil	2.0	125	12.8	2.95	*Proteus vulgaris* sepsis
11-16	Pregestimil	3.0	135	15.6	2.35	...
17-23	Pregestimil	4.0	160	7.6	2.81	...
24-28	Pregestimil	1.6	70	−10.7	2.14	*Proteus* sepsis, diarrhea
29-35	Pregestimil	2.8	115	−5.0	2.82	...
36-40	Pregestimil	4.0	150	9.0	...	Sepsis; death, day 45
	Infant 364, M—15.3 mo, 72 cm, 5.45 kg					
1	IV fluids			22.6	3.19	Dehydration, questionable sepsis
2-5	Pregestimil	1.6	56	6.5	2.10	*E coli* in blood
6-10	Pregestimil	2.5	100	3.8	2.59	Still very sick
11-22	Pregestimil	3.0	100	−2.1	3.40	Infection controlled
23-41	Pregestimil	3.5	150	10.5	4.51	...
42-59	Pregestimil	2.6	140	2.5	4.43	...
	Infant 344, F—17 mo, 71 cm, 5.74 kg					
1-3	IV & oral fluids			37.8	1.34	Diarrhea, dehydration
4-9	Pregestimil	1.6	58	−8.5	1.52	Edema
10-17	Pregestimil	2.8	113	−6.3	1.63	Pneumonitis, diarrhea
18-19	IV fluids + blood			18.6		Still edematous
20-25	Pregestimil	1.6	54	−14.4	2.34	Edema gone
26-58	Pregestimil	3.7	140	5.3	4.02	...
	Infant 345, F—11.4 mo, 65 cm, 4.45 kg					
1-3	IV fluids			12.5	3.51	Diarrhea, acidosis
4-6	Pregestimil	1.1	33	−8.8	2.21	IV amino acids
7-16	Pregestimil	2.6	105	−5.2	...	Diarrhea, *P vulgaris* sepsis
17	IV fluids			4.6	2.19	...
18-25	Pregestimil	2.0	75	9.5	2.44	Suprapubic abscess
26-36	Pregestimil	3.0	140	8.3	3.13	Ascaris, tricocephalus
37-38	Varied diet			−38.6	3.82	Diarrhea
39-44	Pregestimil	2.3	80	12.8	4.01	Giardiasis
45-58	Pregestimil	3.8	150	7.7	4.22	...

clinical condition. Serum albumin level had fallen from 4.27 to 2.17 gm/100 ml. During 16 days of Portagen administration at the same protein and calorie levels, this rose to 4.14 gm/100 ml and he gained 1 kg in weight. A trial administration of milk caused an increase in stool weight and cessation of weight gain. Results of lactose tolerance test (LTT) were flat and Portagen was given again for 15 days, at only 6.4% to 8.0% protein calories, with resumed rapid weight gain and maintenance of normal serum albumin.

Infant 246 had also received the wheat-soy blend during 38 days in progressively increasing amounts, up to 4.5 gm protein and 150 kcal/kg/day. Despite persistent fever and hepatosplenomegaly, she had gained weight steadily but the serum albumin level had fallen from 3.74 to 2.18 gm/100 ml. During 35 days' administration of Portagen at a similar energy level but only 4 gm of protein per kilogram per day, despite continued fever (tuberculin test results became positive), she continued to gain and serum albumin level recovered to 3.45 gm/100 ml. Subsequently, liver biopsy revealed a presumably tuberculous granuloma; with specific therapy the fever and organomegaly disappeared and serum albumin level rose further.

During the first 31 days infant 249 had severe diarrhea, recurrent dehydration and acidosis, episodes of cyanosis, apnea and seizures, polyuria, thrombophlebitis, a bleeding tendency, two instances of *Escherichia coli* bacteremia and sepsis, *Shigella sonnei* in the stool, moniliasis, neutropenia, prolonged prothrombin time, and a fall in serum albumin level from 4.70 to 2.80 gm/100 ml. During 24 days weight had been maintained by the intravenous route, as modified milk, our casein mixture, and even a dextrose-electrolyte mixture had caused diarrhea. During the next seven days an isolated soy protein formula had been tried with some initial success but diarrhea recurred and he lost weight. On the 32nd day, Portagen was cautiously introduced. On the 35th day, a periphlebitic abscess, from which *E coli* was cultured, was drained. Undiluted Portagen was well tolerated, steady weight gain was established, and serum albumin level rose to 4.42 gm/100 ml in 16 days.

Pregestimil was used in the management of four infant girls (infants 328, 346, 348, and 355) with marasmus. Table 2 summarizes the results. During some periods, particularly the initial ones, the intake listed is the average for those days, when the amount given was gradually increased while tolerance was being tested. When oral intake of

protein was still very low, the intravenous fluids contained amino acids, along with the necessary water, electrolytes, and dextrose to meet basal requirements. Infant 355 was discharged against medical advice on the 11th day; she was not yet gaining weight but had established tolerance for the formula. After the characteristic initial fall in serum albumin level, which is the result of rehydration,[10] and perhaps of a lag in synthesis, infants 328, 346, and 348 had a rise in serum albumin level and gained weight steadily.

Table 3 summarizes the results in a 22.4-month-old boy (infant 360) with severe marasmus who received Pregestimil during most of a 105-day period. Initial response was satisfactory; his diet was gradually changed to a milk diet but he subsequently developed bulky stools and finally diarrhea. He was found to have giardiasis and a flat LTT response. Response to Pregestimil was again satisfactory. Convalescence was interrupted by an episode of bloody diarrhea, pneumonia and anemia, and still another episode of pneumonia. On day 106 his diet was changed to a hospital diet.

A 16.6-month-old girl (infant 361) with marasmic kwashiorkor and a staphylococcal infection was treated with Pregestimil in gradually increasing amounts. By the ninth day edema was gone and by the 22nd day serum albumin level had risen to 3.47 gm/100 ml from an initial value of 1.22 gm/100 ml. She was gaining weight steadily and was clinically well. The LTT response was flat but she later tolerated up to 500 ml of cow's milk daily in a mixed diet.

Five malnourished, extremely sick infants (infants 359, 330, 364, 344, and 345) with diarrhea were also given Pregestimil as their oral feeding during most of the initial treatment. Table 4 summarizes the results. Infant 359, admitted with severe diarrhea, dehydration, acidosis, circulatory collapse, and pneumonitis, responded slowly to parenteral therapy. On the fifth day Pregestimil was introduced cautiously and was well tolerated. The subsequent course was uneventful.

Infant 330 tolerated the formula without recurrence of diarrhea but weight gain was rapid and serum albumin level fell considerably, both of which suggested impaired protein synthesis. Blood and urine cultures were positive for *Proteus vulgaris* on day 9; after treatment there was some improvement, but on day 23 there was a recurrence of acute diarrhea and the blood culture was again positive for *Proteus*. A brief period of improvement was followed by an episode of septic shock (probably a *Pseudomonas* superinfection) and eventual death. Even though feedings may be taken well and not produce diarrhea, a severe infection such as was present here prevents proper utilization of amino acids and leads to a severe protein-deficiency state, with hypoalbuminemia, hypotonicity, and extracellular fluid volume expansion.

Infant 364 also demonstrated poor protein utilization until systemic infection was brought under control.

In infant 344, admitted with diarrhea, dehydration, and hypoalbuminemia but no visible edema, initial parenteral management produced improvement but edema became apparent, while fever and signs of pneumonic involvement persisted. A recurrence of diarrhea further delayed recovery. When infection was controlled, her convalescence proceeded smoothly.

Infant 345, also admitted with diarrhea, dehydration, and acidosis, received parenterally administered fluids and amino acids during the first week. Oral feedings were begun on the fourth day and were tolerated well, but during the second week diarrhea recurred and blood culture was positive for *P vulgaris*. Protein utilization was poor until a suprapubic abscess (at the site of a vesical tap) was discovered and drained. She was also treated for *Ascaris*, *Trichuris*, and *Giardia*. An attempt to introduce a milk-containing hospital diet on days 37 and 38 resulted in diarrhea. The LTT response was flat and Pregestimil was reintroduced. On the 59th day, milk was tried again and produced diarrhea, but when the amounts were cut down it was tolerated well.

Comment

Limited comparative studies confirmed the expected high nutritional value of the casein and the casein hydrolysate in the two formulas. They were suggestive of a higher calorie efficiency, possibly the result of better absorption of the MCTs than the vegetable oil. In the other studies, when our casein-sucrose-cottonseed oil mixture briefly replaced one of these two formulas, rates of weight gain at identical calorie intakes were also lower, possibly for the same reason. This slight advantage might be of real value to the very sick, severely malnourished infant.

The good results with Portagen in four cases of uncomplicated kwashiorkor and with Pregestimil in an additional case are not different from those we expect with our casein-sucrose-oil formula. Our results with lactose-containing modified milk have also been good, but in approximately 50% of children with kwashiorkor we have encountered decreased lactose tolerance and have had to dilute the formula with our casein-based mixture for a matter of days or even weeks. We have never encountered sucrose intolerance in this situation, nor have we found poor digestion of protein, so that there seems to be no advantage to the casein hydrolysate or to the glucose of product Pregestimil in this situation.

Rates of increase in serum albumin level were very similar to those reported by Waterlow[11] and ourselves[10] for casein or milk diets. In our experience this was between 17 and 146 mg/100 ml/day, with a mean of

around 60 mg/100 ml/day for similar protein and calorie intakes. For Portagen these rates were 35 to 123 mg/100 ml/day and for the one patient with kwashiorkor who received Pregestimil, it was 102 mg/100 ml/day. The number of days until disappearance of clinical edema was also very similar.

Since energy needs are seldom a problem in kwashiorkor, the advantages of the MCTs are probably outweighed by the higher cost. Although casein-sucrose-vegetable oil mixtures can be put together at a low cost, there are other advantages to a product such as Portagen. Errors or omissions of concept or of preparation in the addition of electrolytes can have disastrous consequences. The commercial vitamin mixtures generally available are not as complete as the one in this product. The trace minerals present in this preparation are also not put together easily. Severely malnourished infants are commonly depleted of trace nutrients without overt evidence of depletion until an adequate or generous supply of protein and energy is made available. In extensive experience with our own feeding mixtures we successively encountered acute magnesium deficiency, inadequate niacin intake, probable zinc deficiency, and probable zinc toxicity.

The infant who was severely hypoalbuminemic after 51 days of a wheat-soy blend diet (infant 244) would undoubtedly have responded as well to our casein-based mixture or to isolated soy protein milk.[12] He did have lactose intolerance but this was probably transient. The second infant (infant 246), who had the tuberculous granuloma, would probably have responded as well to modified milk or other high-quality products. The third infant (infant 249), who had probable transient intolerance to all carbohydrates at one point, responded to Portagen after the isolated soy protein milk had not been well tolerated. His situation is more difficult to explain; this response may have been coincidentally due to the clearing up of his infection, or may represent better tolerance of the MCTs than of vegetable oil, or of the relatively lower sucrose content of Portagen.

The results with Pregestimil in the four infants with marasmus would probably have been matched by Portagen or even modified milk, although the establishment of tolerance and weight gain, while maintaining improvement of serum albumin levels after the initial fall, was more prompt than usually experienced in our unit. In the older boy with marasmus, because of his age, relative lactase deficiency was to be expected and was indirectly documented. The bulky stools, with increased stool fat, may have been due to the *Giardia* infection.

In the five infants with severe diarrhea and malnutrition we would almost certainly have encountered two or three with severe transient deficiency of lactase and possibly other disaccharidases. Fortunately, none had glucose malabsorption and Pregestimil was tolerated well, without producing recurrence of the diarrhea. When severe systemic infection is present, one cannot expect adequate protein synthesis and this was well demonstrated in these examples. A disaccharide-free formula may well be of value in such a situation but our studies did not prove this, as lactose and other disaccharide tolerance tests were not done. One is understandably reluctant to carry out tests in such sick infants but on the other hand, it might be safer to do so, using a reduced load, than to discover intolerance through an injudicious attempt to feed disaccharide-containing formulas.

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