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Nutrition Protocol for Management of Inborn Errors of Metabolism

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Preface

Inborn errors of metabolism (IEM), are inherited conditions caused by deficiency of specific enzymes essential for the body's cell function. This may lead to the accumulation of toxic metabolite(s) that cause serious damage to vital organs or cause biochemical or electrolyte imbalance.

IEM disorders are rare individual diseases but are common as a group of diseases. The incidence rate is around 1 per 1000 births. These disorders usually manifest early in life with clinical or biochemical modifications that may not be recognized early. Often times the damage is irreversible, and the best way to manage these children is to screen them before they show such signs or symptoms. Diagnosed cases are registered and special diet, drug therapy and/or enzyme replacement is provided to maintain normal metabolism.

Nutritional Management plays an essential role in the management of several of these disorders. The aim of dietary management includes: normal weight gain, linear growth, head growth and psychomotor development, as assessed by serial examinations and valid developmental screening tools (e.g., Denver Developmental Screening Test II). Metabolic dietitian in coordination with metabolic genetic consultant and the family are the stakeholders of management of these conditions.

The protocols in this manual are intended to serve as guides for health care professionals who treat infants, children, adolescents and adults with inherited metabolic disorders. They will be particularly useful to those who are relatively unfamiliar with nutrition support of metabolic disorders, although specialists working in treatment centers where protocols are already established should find them useful as well.

Chapter 1

Nutritional Support for Urea Cycle Disorders

Introduction:

The Urea Cycle Disorders (UCDs) referred to diseases that result from the defects in the metabolism of waste nitrogen that comes from the breakdown of the protein and any other molecules contain nitrogen, which enter to urea cycle to convert ammonia to their end product urea that will be eliminated in urine.

There are six known types of UCDs

1. Carbamoyl Phosphate Synthetase deficiency (CPS1)
2. Ornithine Transcarbamylase deficiency (OTC)
3. N-Acetylglutamate Synthase deficiency (NAGS)
4. Argininosuccinate Synthetase deficiency (ASS)
5. Argininosuccinate Lyase deficiency (ASL)
6. Arginase deficiency (ARG)

Clinical Features:

Sever deficiency or total absence of any of the first five enzymes (CPS1, OTC, NAGS, ASS and ASL) result in elevation of ammonia level and other precursors metabolites in the first few days of life, which may lead rapidly to develop

cerebral edema and other related signs of lethargy, anorexia, hypothermia, hypo or hyperventilation, seizures, encephalopathy and coma.

In ARG deficiency, ammonia elevation happen during illness or stress at any time of life, and other neurological features e.g. spastic paraplegia

In late diagnosed cases or cases with poor compliance to diet, frequent uncontrolled hyperammonemia may lead to more neurological manifestations including developmental delay, seizures and permanent neurological insults.

Diagnosis:

The diagnosis of UCDs is a combination of clinical suspicion and biochemical abnormalities which ultimetly needs molecular genetic testing to confirm it. Classically, in any neonate with lethargy and in absence of impaired liver function Ammonia concentration of >150 umol/L with normal anion gap is a strong indication for UCDs. This can be associated with respiratory alkalosis.

Quantitative Plasma Amino Acid (PAA) analysis, arganinosccinic level and measurement of urine orotic acid can differentiate between specific UCDs.

Definitive diagnosis of UCDs depends on either molecular genetic testing or enzyme activity assays.

Genetic Counseling:

All UCDs are inherited as autosomal recessive except OTC deficiency that inherited as X-linked manner. Carrier testing and prenatal diagnosis are possible for all UCDs if the pathogenic mutation in the family is known.

Management:

Decompensation caused by catabolic stress (e.g. vomiting, diarrhea, febrile illness and decreased oral intake) management of UCDs can be classified as

- **Acute Management**
- **Chronic management**

Acute Management: acute sever hyperammonemia needs to be managed immediately and aggressively using administration of high caloric intake (IVF 10% Dextrose and IV lipids), and Intravenous arginine hydrochloride and nitrogen scavengers drugs (Na benzoate and Na phenylacetate) to allow alternative pathway excretion of excess nitogen. Keeping patients NPO for 12-24 hours and may be more, lead to restriction of protein to reduce the nitrogen amount in the diet.

In case of severe hyperammonemia >500umol/L hemodialysis (CRRT) must be considered for rapid decrease of ammonia.

Chronic Management: long term management and monitoring always needed to prevent catabolism during illness to prevent hyperammonemia episodes by dietary

restriction of protein, use of special formulas, oral arginine hydrochloride and nitrogen scavenger agents.

Liver transplant has been successfully tried in number of affected individuals.

Nutritional support for urea cycle disorders

Restrict the dietary protein to amount that can be tolerated without causing hyperammonemia and excessive body protein catabolism.

The goals of nutrition management:

- Maintain plasma amino acids and ammonia within normal range for age. (Table 1a&1b)
- Support normal growth rate in infants and children and maintain appropriate weight for height in adults.

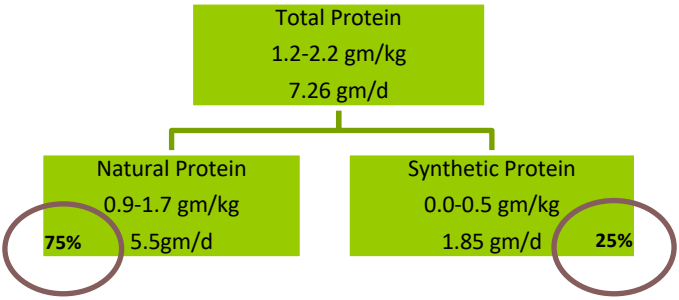
Calculation:

- **What to calculate** (All examples for 3.3kg infant)

  1. Protein:

  Determine the amount of protein needed as per age and weight (Table 2)

  Example: 0 – 1 Years:



2. Energy:

   Prescribe a good amount greater than the RDA to prevent catabolism (Table -2)

120-145 kcal/kg/d → 135 kcal/kg/d → 445 kcal/d

- **How to calculate**

Nutrition Requirement:

Energy	125-150 kcal/kg	135 kcal/kg
Protein	1.2-2.2 gm/kg	2.2 gm/kg
Natural Protein	75%	5.5 gm/kg
Synthetic protein	25%	1.85 gm/kg

1. Protein:
   a) Calculate the amount of infant formula (similac)/whole cow's milk required to fill 75% of the total protein prescribed (Table-3)

1gm similac = 0.118gm protein
47gm similac = **5.5gm protein**

We need 5.5gm protein/d

b) Supply the remaining protein 25% with Cyclinex-1 (for infant and toddlers) Cyclinex-2 (for children, adolescents, and adults). (Table-4)

100gm cyclinex-1 = 7.5gm protein
24gm cyclinex-1 = **1.85gm protein**

We need
1.85gm protein/d

2. Energy :

a) Calculate energy provided by infant similac/whole cow's milk and Cyclinex-1 to fill protein requirement. (Table 3&4)

1gm similac 5.26kcal	100gm cyclinex-1 510kcal
⇩	⇩
47gm similac 247kcal	24gm cyclinex-1 122kcal

b) Subtract amount determined above from total energy prescription

445-247-122 = 76 kcal (Remained)

c) Provide any remaining energy with Prophree (5.2 kcal/g) OR Polycose (3.8 kcal/g)

1gm prophree = 5.2 kcal
14.5gm prophree= **76 kcal**

We need
76 kcal/d

d) Add sufficient water to provide between 20kcal/oz to 30kcal/oz

20 kcal = 30ml
456 kcal = 684ml

Total Volume
684ml

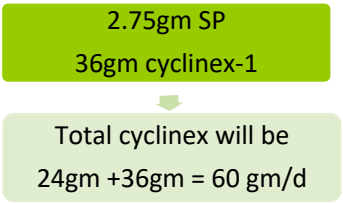
e) Refrigerate in sterilized, closed container until used.
f) Feed infant 8-10 times/day, older child 4-6 times/day, and discard unused formula after 24 hrs. (The feed will be 70-60 ml q3-2 hrs)

Provide parents, caregiver with completed Diet Guide with each diet change

Sick day's management: (50% Natural Protein)

1. Reduce natural protein intake to 50% for 24-48 hrs.

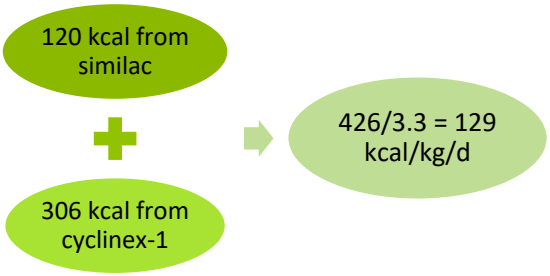
   50% of Similac:
   23gm similac = 2.75gm protein.



2. Add the other 50% protein removed from similac as synthetic protein (cyclinex-1).

   Total protein intake (Natural + synthetic) will be 7.26 gm/d

3. Check the total energy



4. Add water to make 20 kcal/oz

20 kcal = 30ml
426 kcal = 639ml

Total Volume
639ml

0 % Natural Protein:

1. Provide all amount of protein needed per day from synthetic protein

Protein needed per day 7.26 gm/d
100gm cyclinex-1 = 7.5gm protein

2. The calorie from cyclinex-1

100gm cyclinex-1 = 510 kcal
(510 kcal/3.3kg = 154 kcal/kg/d)

Examples summary:

New born baby with UCD weigh: 3.3kg

Nutrients Requirements:	Give:
• Energy: 125-150 kcal/kg	135 kcal/kg
• Protein: 1.2-2.2 g/kg	2.2 gm/kg
• Natural Protein: 75%	5.5 gm/kg
• Synthetic protein: 25 %	1.85 gm/kg

100% NP	Amount gm	Protein		Energy
		N.P.	AA	
Similac	47	5.5		247
Cyclinex-1	24		1.8	122
Prophree	14.5			76
Total/d		5.5	1.8	456
Total/kg		1.6 (75%)	0.6 (25%)	135

Fluids: add water to make total volume of 675ml

50% NP	Amount gm	Protein		Energy
		N.P.	AA	
Similac	23	2.71		120
Cyclinex-1	60		4.5	306
Total/d		2.71	4.5	426
Total/kg		2.18		129

Fluids: add water to make total volume of 645ml

Monitoring and Evaluation:

1. Anthropometrics:
   Monitor weight and height every 3 months

2. Dietary evaluation:
   3 days dietary recall for protein and energy intake before clinic visit, if patient eating solid food (Table 5)

3. Laboratory :
   - Hgb, albumin, pre albumin, zinc
   - Ammonia level
   - Plasma amino acid profile :

- Glutamine: if high, decrease protein and increase energy.
- Alanin: if high, increase energy intake.
- Glycine: if high, increase energy intake.
- Valine, isolucine and leucine:
  - ✓ If low, increase Natural protein.
  - ✓ If high, decrease Natural protein.

Table 1a: (Normal ammonia level by age)

Age	Upper limit (µmol/l)
0-7 day	**94**
8-30 days	**80**
1 m-15yr	**48**
>16	**26**

Table 1b: (Treatment ranges for target amino acids in urea cycle disorders)

Amino Acid (µmol/l)	(2-4 hrs postprandial)			
	Newborn	1-3 m	3m-6y	6-18y
GLYCINE	106-254	105-222	125-318	158-302
ALANINE	132-455	134-416	148-475	193-545
GLUTAMINE	243-822		475-746	360-740
LYSINE	71-272	37-168	85-218	108-233
ARGININE	17-119	21-74	32-142	44-130
ISOLEUCINE	27-80	32-87	13-81	38-95
LEUCINE	61-183	43-165	40-158	79-174
VALINE	78-264	96-291	85-334	156-288
CITRULLINE	3-36	6-36	8-47	19-52

Table 2: Recommended ranges for nutrients and drug treatment for urea cycle disorders:

	Age (Years)	Total protein (g/kg/day)	Protein Eq EAA Mixture (g/kg/day)	Natural protein (g/kg/day)	Energy (kcal/kg/day)
Carbamoyl phosphate synthetase	0 < 1	1.2 – 2.2	0.6 – 1.1	0.6 – 1.1	120 - 145
	0 < 7	1 – 1.2	0.6 – 0.7	0.4 – 0.5	100 - 120
	7 < 19	0.7 – 1.4	0.4 – 0.7	0.3 – 0.7	80 - 110
	≥ 19	0.5 – 1	0.3 – 0.5	0.2 – 0. 5	35 - 65
Ornithine transcarbamylase	0 < 1	1.2 – 2.2	0.6 – 1.1	0.6 – 1.1	120 - 145
	0 < 7	1 – 1.2	0.6 – 0.7	0.4 – 0.5	100 - 120
	7 < 19	0.7 – 1.4	0.4 – 0.7	0.3 – 0.7	80 - 110
	≥ 19	0.5 – 1	0.3 – 0.5	0.2 – 0. 5	35 - 65
Argininosuccinate synthetase (citrullinemia)	0 < 1	1.2 – 2.2	0.0 – 0.5	0.9 – 1.7	120 - 145
	0 < 7	1 – 1.2	0.0 – 0.3	0.7 – 0.9	100 - 120
	7 < 19	0.7 – 1.4	0.0 – 0.3	0.4 – 1.1	80 - 110
	≥ 19	0.5 – 1	0.0 – 0.2	0.3 – 0.8	35 - 65
Argininosuccinate lyase (ASL)	0 < 1	1.2 – 2.2	0.0 – 0.5	0.9 – 1.7	120 - 145
	0 < 7	1 – 1.2	0.0 – 0.3	0.7 – 0.9	100 - 120
	7 < 19	0.7 – 1.4	0.0 – 0.3	0.4 – 1.1	80 - 110
	≥ 19	0.5 – 1	0.0 – 0.2	0.3 – 0.8	35 - 65
Arginase	0 < 1	1.2 – 2.2	0.0 – 0.5	0.9 – 1.7	120 - 145
	0 < 7	1 – 1.2	0.0 – 0.3	0.7 – 0.9	100 - 120
	7 < 19	0.7 – 1.4	0.0 – 0.3	0.4 – 1.1	80 - 110
	≥ 19	0.5 – 1	0.0 – 0.2	0.3 – 0.8	35 - 65

Table 3: Natural protein analysis

	Leucin (mg)	Isoleucine (mg)	Methionine (mg)	Tryptophan (mg)	Phenylalanine (mg)	Threonine (mg)	Lysine (mg)	Valine (mg)	Protein (mg)	Energy (mg)
Human milk 30 ml	**21**	**17**	**6**	**5**	**14**	**14**	**21**	**19**	**-**	**-**
Soybean milk 240 ml	802	460	142	134	513	463	708	489	-	-
Whole milk 1 ml	**3.29**	**2.03**	**0.85**	**0.47**	**1.62**	**1.52**	**2.66**	**2.24**	**0.0336**	**0.62**
Low fat milk 1 ml	3.2	2	0.009	0.41	1.6	1.5	2.6	2.2	0.03	0.7
Skimmed milk 1 ml	3.34	2.06	0.86	0.48	1.65	1.54	2.7	2.28	0.034	0.35
Nido/whole milk powder 1 gm	25.7	15.9	6.5	3.9	12.7	11.8	20.8	17.6	0.26	4.9
Skimmed milk powder 1 gm	35.4	21.8	9	5.1	17.4	16.3	28.6	24.2	0.36	3.6
Whole yogurt plan 1ml	3.3	1.79	0.96	0.18	1.79	1.34	2.9	2.7	0.03	0.6
Low fat yogurt plan 1 ml	5	2.7	1.46	0.27	2.7	2.03	4.45	4.1	0.05	0.6
Skim yogurt plan 1 ml	5.4	2.9	1.59	0.3	2.9	2.2	4.8	4.4	0.05	0.5
Isomil 1 gm powder	10.75	5.78	3.19	1.63	6.75	4.93	7.54	5.82	0.137	5.17
Similac 1 gm powder	**10.32**	**5.36**	**2.71**	**1.51**	**4.6**	**5.53**	**8.4**	**5.7**	**0.118**	**5.26**
Pediasure 1 ml	**2.776**	**1.48**	**0.804**	**-**	**-**	**1.34**	**-**	**1.764**	**0.03**	**1**
Whole egg 50 gm	533	380	196	97	343	298	4.1	4.37	6.07	79
Cream cheese 20 gm	207	113	51	19	119	91	192	125	2.1	99
Coconut fresh shredded ½ cup	130	87	34	16	48	62	73	103	-	-
Peanut butter 1 tbs	272	148	39	0	227	120	160	223	-	-
Lentil cooked 2/² cup 100 gm	554	413	55	10	359	273	476	421	-	-
Thyme (za'atar)	6	7	0	3	0	4	3	7	-	-
Mustard	59	36	16	17	35	36	50	44	-	-
Sesame seeds 23 gm	443	250	168	87	387	188	153	234	-	-

Fenugreek seed 1 tebs/4 gm	65	45	13	14	40	33	62	41	-	-
Farina rice cereal 1 cup / 100 gm	1130	690	260	180	475	645	945	720	-	-
Corn flour 110 gm / 1 cup	1118	396	163	52	387	344	249	139	-	-
Rice flour 125 gm / 1 cup	645	352	135	82	375	292	292	525	-	-
All-purpose flour 11 tbs	719	364	186	129	526	285	235	432	10.5	365
20 tbs cocoa – no milk or sugar	372	241	61	100	303	241	317	363	18	280
Potato chips 20 gm	55	48	13	11	48	45	58	58	1.1	113

Table 4: Nutrient composition of cyclinex-1 and cyclinex-2

Nutrient	Cyclinex-1		Cyclinex-2	
	(per 100 g pwd)	(per g protein equiv)	(per 100 g pwd)	(per g protein equiv)
Energy, kcal	510	68	440	32
Protein equiv, g	7.50	1.000	25.00	1.000
Nitrogen, g	1.20	0.160	2.40	0.160
Amino acids, g	9.65	1.287	19.30	1.287
Cystine, g	0.30	0.040	0.60	0.040
Histidine, g	0.36	0.048	0.72	0.048
Isoleucine, g	1.28	0.170	2.56	0.170
Leucine, g	2.17	0.289	4.34	0.289
Lysine, g	1.11	0.148	2.22	0.148
Methionine, g	0.34	0.045	0.68	0.045
Phenylalanine, g	0.75	0.100	1.50	0.100
Threonine, g	0.75	0.100	1.50	0.100
Tryptophan, g	0.28	0.037	0.56	0.037
Tyrosine, g	0.88	0.117	1.76	0.117
Valine, g	1.43	0.190	2.86	0.190
Other Nitrogen-Containing Compounds				
L-Carnitine, mg	190	25.00	370	24.67
Taurine, mg	40	5.3	60	4.00
Carbohydrate, g	57.0	7.60	45.0	3.00
Fat, g	24.6	3.28	17.0	1.13
Linoleic acid, g	2.00	0.266	1.82	0.121
α-Linoleic acid, g	0.41	0.055	0.28	0.019
Minerals				
Calcium, mg	650	86	1,150	77
Chloride, mg/mEq	390/11.00	52.0/1.47	1,325/37.37	88.3/2.49
Chromium, µg	12	1.60	37	2.47
Copper, mg	1.25	0.167	1.30	0.09
Iodine, µg	80	10.67	150	10
Iron, mg	10.0	1.33	17.0	1.13
Magnesium, mg	55	7.3	300	20.0
Manganese, mg	0.50	0.067	1.00	0.07

Molybdenum, µg	13	1.73	40	2.67
Phosphorus, mg	455	60	1,020	68
Potassium, mg/mEq	760/19.44	101/2.59	1,800/46.03	120/3.07
Selenium, µg	25	3.33	37	2.47
Sodium, mg/mEq	215/9.35	28.7/1.25	1,175/51.11	78.3/3.41
Zinc, mg	9.5	1.27	17.0	1.13
Vitamins				
A, µg RE	480	64	908	61
D, µg	7.50	1.00	8.12	0.54
E, mg α-TE	11.40	1.52	16.11	1.10
K, µg	60	8.0	70	4.67
Ascorbic acid, mg	60	8	75	5
Biotin, µg	75	10	150	10
B_6, mg	0.85	0.113	1.75	0.12
B_{12}, µg	5.60	0.750	7.30	0.487
Choline, mg	100	13.3	130	8.7
Folate, µg	250	33.00	530	35.33
Inositol, mg	50	6.7	110	7.316.70
Niacin equiv, mg	16.70	2.23	30.3	2.02
Pantothenic acid, mg	7.80	1.040	10.90	0.726
Riboflavin, mg	1.0	0.133	2.4	0.160
Thiamin, mg	2.0	0.267	4.0	0.267

Table 5: serving lists for protein – restricted diets: Approximate Nutrient Content per Serving

Food list	**Nutrient**	
	Protein (g)	Energy (kcal)
Breads/Cereals	0.6	30
Fats	0.1	60
Fruits	0.5	60
Vegetables	0.5	10
Cyclinex-1®100gm	7.50	510
Cyclinex-2 ®100gm	15.00	440

 Urea Cycle Disorders

Chapter 2

Nutritional Support for Propionic & Methylmalonic Acidemia

Introduction:

Propionic acidemia (PA) and methylmalonic acidemia (MMA) are two known disorders belong to organic aciduria (OA) disorders which characterized by excessive excretion of non-amino organic acids in urine.

PA and MMA are caused by deficiency of two enzymes called propionyl CoA carboxylase and methymalonyl-CoA mutase respectively lead to dysfunctions of specific step in amino acid catabolism namely branched chain amino acid.

Clinical Features:

The usual clinical presentation is toxic encephalopathy and include vomiting, poor feeding, neurological symptoms such as seizures and abnormal tone and lethargy which may progress to coma. Typically the presentation at neonatal periods which may lead to misdiagnosis as neonatal sepsis, outcome is enhanced by early detection and recognition and treatment in the first ten days of life.

Diagnosis:

Clinical laboratory finding that support the diagnosis of PA and MMA include high anion gap metabolic acidosis, ketosis, hyperammonemia, abnormal liver function test, hypoglycemia and neutropenia.

First line diagnosis in PA and MMA is urine organic acid analysis using gas chromatography mass spectrometry (GC/MS) and Acylcarnitine profile using tandem mass spectrometry (Tandem MS).

Confirming testing involves assay of enzymatic activities in lymphocyte, cultured fibroblast or by molecular genetic testing.

Genetic Counseling:

PA and MMA are inherited as autosomal recessive manner, at conception; the mother of affected proband has 25% chance of having another affected child. Carrier testing and prenatal diagnosis is possible if the pathogenic mutation in the family is known.

Management:

Decompensation caused by catabolic stress (e.g. vomiting, diarrhea, febrile illness and decreased oral intake) management of PA and MMA can be classified as

- **Acute Management**
- **Chronic management**

Acute Management: acute sever hyperammonemia and acidosis needs to be managed immediately and aggressively using administration of high caloric intake (IVF 10% Dextrose and IV lipids). Carbaglu (carglumic Acid) and Intravenous arginine hydrochloride and nitrogen scavengers drugs (Na benzoate and Na phenylacetate) to allow alternative pathway excretion of excess nitogen. Keeping patients NPO for 12-24 hours and may be more, lead to restriction of protein to reduce the nitrogen amount in the diet.

In case of sever hyperammonemia, >500 µmol/L, hemodialysis (CRRT) must be considered for rapid decrease of ammonia.

Chronic Managemen: long term management and monitoring always needed to prevent catabolism during illness to prevent hyperammonemia episodes by dietary restriction of protein, use of special formulas, oral biotin (as cofactor) for PA, and cycles of metronidazole (monthly) to clear the normal flora from the gut which may play role as endogenous source of ammonia production.

Nutritional support for Propionic & Methylmalonic Acidemia

Propionic academia (PA) and Methylmalonic academia (MMA) are disorders of essential Isoleucine (ILE), Methionine (MET), Threonine (THR), and Valine (VAL) and odd-chain-fatty acid metabolism. The nutritional therapy for PA and MMA is the same.

The goals of nutritional management:

1. Provide all essential nutrients to promote normal physical and mental development
2. Maintain adequate intake of restricted ILE, MET,THR,VAL and other essential nutrients to support anabolism and prevent deficiencies
3. Limit fasting and maintain adequate hydration
4. Provide aggressive medical and nutrition intervention during critical illness.

Calculation:

- **What to calculate:**
  1. ILE, MET, THR, VAL
     a) Prescribe intakes that promote goals of nutrition support from natural source (infant formula, regular milk, solid food)
     b) Requirements vary widely; from patient to patient and in the same patient depending on age, growth rate , adequacy of energy and protein intakes and state of health.

2. Protein:

   Prescribe amount greater than RDA, from both natural and synthetic source.

3. Energy:

   Prescribe amount that should support normal weight gain in infants and children and maintain appropriate weight for height in adults.

4. Fluid:

   Prescribe amount that will supply water requirement, normally 1.5 ml fluid for neonates and 1ml fluid for children and adults for each kcal ingested.

5. Odd-Chain-Fatty Acid:

   Avoid dietary sources of odd-chain-fatty acids, including butter, cream, olive oil, excess polyunsaturated fatty acids.

   Inhibit catabolism and loss of adipose tissue by maintaining adequate nutrition status and preventing weight loss.

- **How to calculate :** (All examples for 3kg infant)

Energy	95-145 kcal/kg	390 kcal /d
Protein	2.5-3.5 gm/kg	10.5 gm/d
Valine	75-105 mg/kg	315 mg/d
Methionine	30-50 mg/kg	150 mg/d
Isolucine	75-120 mg/kg	360 mg/d
Thrionine	75-135 mg/kg	405 mg/d

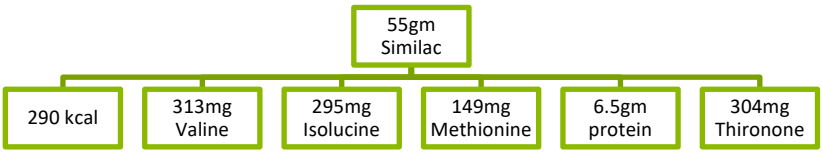
1. Protein :
   a) Initiate protein prescription with highest recommended intake for age.(table 1)

   Example: 0 – 3 month

   Total protein 2.5-3.5 gm/kg
   10.5 gm/d

   b) Calculate amount of infant formula, skim milk, or table food required to fill ILE, MET, THR and VAL (Table 1)
   - Valine 75-105 mg/kg/d = 315 mg/d
   - Methionine 30-50 mg/kg/d = 150 mg/d
   - Isolucine 75-120 mg/kg/d = 360 mg/d
   - Thrionone 75-135 mg/kg/d = 405 mg/d

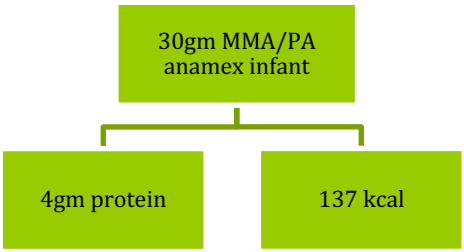
Table 5



c) Subtract amount determined above from the total protein prescription.

(10.5 gm/d - 6.5 gm/d = 4 gm/d)

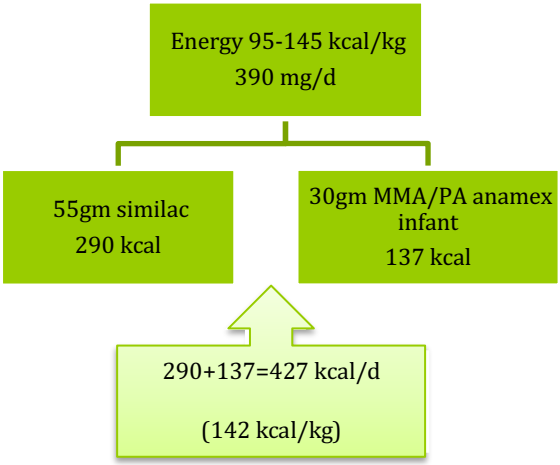
d) Supply any remaining prescribed protein with synthetic protein.
- Propimex-1(abbot), MMA/PA anamex infant (nutricia) for infant and toddlers. (Tables 2&3)
- Propimex-2 (abbot), XMTVI Maxamaid (nutricia) are for children and adults. (Tables 2&3)



e) Weight the powder on scale that reads in grams.
- Either ILE or VAL in formula may be used as a marker to determine Natural protein required.

2. Energy:
   a) Calculate energy provided by infant formula and synthetic protein required to fill protein prescription (Table 1, 3, 5)

Example: 0 – 3 month:



b) Subtract amount determined above from total energy prescription

c) Provide remaining prescribed energy with Ploycose (3.8 kcal/gm) or Pro-Phree (5.2 kcal/gm)(if needed)

3. Fluid :

a) Add sufficient water to infant formula, synthetic protein and the energy supplement and mix in sterilized, tightly closed container by shaking for 10 to 12 seconds.

Add water to make total volume of 500 cc/day

b) Refrigerate in sterilized, closed containers until used and discard unused formula after 24 hours.

c) Feed young infants 6-8 times daily, feed children and adults 4-6 times daily.
d) Provide parents, caregiver with completed Diet Guide.

Monitoring & Evaluation of Nutritional Support:

1. GLY is often elevated in patients with PA or MMA, improvement suggests better metabolic control.
2. Plasma GLY ,ILE, MET, THR, and VAL concentration:
   a) If it's low Increase prescribed amount of natural protein by 10% to 25% and reevaluate plasma concentration in 3 days, repeat above process until value is in treatment range.
   b) Individual supplementation of one of the amino acids may be required. If high, decrease prescribed amount of natural protein by 5% to 10% and reevaluate plasma concentration in 1 week, repeat above process until value is in treatment range.
3. Growth status: Monitor weight and height with every clinic visit and must be plot on NCHS growth charts if patient remains below usual growth channel and does not respond to increase in protein and energy or cannot

consume diet prescribed through oral feeding, nasogastric or gastrostomy tube feeding should be considered.

Example:

New born baby with MMA/PA weight 3.0kg

Nutrients Requirements:	Give:
• Energy: 95-145 kcal/kg/d	390 mg/d
• Protein: 2.5-3.5 gm/kg/d	10.5 gm/d
• Valine: 75-105 mg/kg/d	315 mg/d
• Methionine: 30-50 mg/kg/d	150 mg/d
• Isolucine: 75-120 mg/kg/d	360 mg/d
• Thrionine: 75-135mg/kg/d	405 mg/d

100% NP	Amount (gm)	VAL (mg)	MET (mg)	ILE (mg)	THR (mg)	Protein		Energy Kcal
						NP gm	AA gm	
Similac	55	313	149	295	304	6.5		290
MMA/PA anamix infant	30						4.0	137
Total/d		313	149	295	304	10.5		427
Total/kg		104	50	98	101	3.5		142

Fluids: add water to make total volume of 650 ml/day

50 % NP	Amount (gm)	VAL (mg)	MET (mg)	ILE (mg)	THR (mg)	Protein		Energy Kcal
						NP gm	AA gm	
Similac	23					2.7		120
MMA/PA anamix infant	46						6.0	210
Total/d						8.7		330
Total/kg		104	50	98	101	3.48		132

Fluid: add water to make total volume of 500 ml/day

Table 1: Recommended daily nutrient intakes (range) for infants, children and adults with Propionic or Methylmalonic Acidemia

Age	Nutrient						
	ILE [1,2] (mg/kg)	MET [1,2] (mg/kg)	THR [1,2] (mg/kg)	VAL [1,2] (mg/kg)	Protein [2] (g/kg)	Energy [2] (kcal/kg)	Fluid[4] (mL/kg)
Infants							
0 to <3 mo	75-120	30-50	75-135	75-105	3.50-2.50	(130)95-145	125-200
3 to <6 mo	65-200	20-45	60-100	65-90	3.50-2.50	(125)95-145	130-160
6 to <9 mo	50-90	10-40	40-75	35-75	3.50-2.50	(120)80-135	125-145
9 to <12 mo	40-80	10-30	20-40	30-60	3.50-2.50	(115)80-135	120-135
Girls & Boys	**(mg/day)**	**(mg/day)**	**(mg/day)**	**(mg/day)**	**(g/day)**	**(kcal/day)**	**(mL/day)**
1 to <4 yr	485-735	180-390	415-600	550-830	≥ 30.0	1,300(900-1800)	900-1,800
4 to <7 yr	630-960	255-510	540-780	720-1,080	≥ 35.0	1,700(1300-2300)	1,300-2,300
7 to <11 yr	715-1,090	290-580	610-885	815-1,225	≥ 40.0	2,400(1650-3300)	1,650-3,300
Women							
11 to <15 yr	965-1,470	390-780	830-1,195	1,105-1,655	≥ 55.0	2,200(1500-3000)	1,500-3,000
15 to <19 yr	965-1,470	275-780	830-1,195	1,105-1,655	≥ 55.0	2,100(1200-3000)	1,200-3,000
≥ 19 yr	925-1,410	265-750	790-1,145	790-1,585	≥ 50.0	2,100(1400-2500)	1,400-2,500
Men							
11 to <15 yr	540-765	290-765	810-1,170	1,080-1,515	≥ 50.0	2,700(2000-3700)	2,000-3,700
15 to <19 yr	670-950	475-950	1,010-1,455	1,345-2,015	≥ 65.0	2,800(2100-3900)	2,100-3,900
≥ 19 yr	1,175-1,190	475-950	1,010-1,455	1,345-2,015	≥ 65.0	2,900(2000-3300)	2,000-3,300

Table 2: Nutrient composition of propimex-1 and propimex-2

Nutrient	Propinex-1		Propinex-2	
	(per 100 g pwd)	(per g protein equiv)	(per 100 g pwd)	(per g protein equiv)
Energy, kcal	480	32	410	13.7
Nitrogen, g	2.40	0.160	4.80	0.160
Protein equiv, g	15.00	1.000	30.00	1.000
Amino acids, g	16.17	1.078	32.34	1.078
Cystine, g	0.45	0.030	0.90	0.030
Histidine, g	0.42	0.028	0.84	0.028
Isoleucine, g	0.12	0.006	0.24	0.008
Leucine, g	1.38	0.092	2.76	0.092
Lysine, g	1.00	0.067	2.00	0.067
Methionine, g	Trace	0	Trace	0
Phenylalanine, g	0.88	0.057	1.76	0.057
Threonine, g	0.10	0.007	0.20	0.007
Tryptophan, g	0.17	0.011	0.34	0.011
Tyrosine, g	0.89	0.059	1.78	0.059
Valine, g	trace	0	trace	0

Other Nitrogen containing Compounds				
Carnitine, mg	900	60	1,800	60
Taurine, mg	40	2.66	50	1.67
Carbohydrate, g	53.0	3.53	35.0	1.17
Fat, g	21.7	1.45	13.0	0.43
Linoleic acid, g	2.00[4]	0.133	2.00[9]	0.07
α-Linoleic acid, g	0.36[6]	0.024	0.17[7]	0.006
Minerals				
Calcium, mg	575	38	880	29
Chloride, mg/mEq	410/11.56	27/0.77	1,160/32.72	38.7/1.09
Chromium, µg	11	0.73	27	0.90
Copper, mg	1.10	0.073	1.00	0.033
Iodine, µg	65	4.33	100	3.33
Iron, mg	9.0	0.6	13.0	0.43
Magnesium, mg	50	3.33	225.	7.5
Manganese, mg	0.50	0.033	0.80	0.027
Molybdenum, µg	12	0.80	30	1.00
Phosphorus, mg	400	27	760	25
Potassium, mg/mEq	675/17.26	45/1.15	1370/35.04	45.7/1.17
Selenium, µg	20	1.33	35	1.17
Sodium, mg/mEq	190/8.26	12.7/	880/38.28	29.3/1.28
Zinc, mg	8.0	0.55	13	0.43
Vitamins0.53				
A, µg RE	420	28	660	22
D, µg	7.50	0.50	7.50	0.25
E, mg α-TE	10.10	0.67	12.10	0.40
K, µg	50	3.33	60	2.00
Ascorbic acid, mg	50	3.33	60	2.00
Biotin, µg	65	4.3	100	3.33
B_6, mg	0.75	0.05	1.30	0.043
B_{12}, µg	4.90	0.33	5.00	0.167
Choline, mg	80	5.3	100	3.33
Folate, µg	230	15	430	14.33
Inositol, mg	40	2.7	70	2.33
Niacin equiv, mg	12.8	0.85	21.7	0.72
Pantothenic acid, mg	6.90	0.46	8.00	0.267
Riboflavin, mg	0.90	0.06	1.80	0.060
Thiamin, mg	1.90	0.127	3.25	0.108

Table 3: Nutrient composition of MMA/PA ANAMEX infant and XMTVI MAXAMAID

MMA/PA ANAMIX INFANT			
Average contents	**Unit**	**per 100g**	**per 100ml**
Energy	Kcal	457	69
	kJ	1915	287
Protein (amino acids)	g(g)	13.1(15.5)	2.0(2.3)
Carbohydrate	g	49.5	7.4
Sugars	g	7.4	1.1
Lactose	g	1.6	0.24
Fat	g	23	3.5
Saturates	g	7.5	1.1
Monosturates	g	9.4	1.4
Polyunsaturates	g	5	0.75

DHA	g	0.07	0.01
LCT	%	97	-
LA/ALA	ratio	6.3:1	-
% energy linoleic acid	%	8.1	-
% energy linoleic α-acid	%	1.3	-
Dietary fibre	g	5.3	0.8
Minerals			
Sodium	mg(mmol)	191 (8.3)	28.7(1.2)
Potassium	mg(mmol)	501 (12.8)	75.2(1.9)
Chloride	mg(mmol)	355(10.1)	53.3(1.5)
Calcium	mg(mmol)	410(10.2)	61.5(1.5)
Phosphorus	mg(mmol)	300(9.7)	45(1.5)
Magnesium	mg(mmol)	58(2.4)	8.7(0.36)
Iron	mg	8.1	1.2
Zinc	mg	5.7	0.86
Copper	µg	430	64.5
Manganese	mg	0.43	0.06
Fluoride	mg	-	-
Molybdenum	µg	12	1.8
Selenium	µg	15.5	2.3
Chromium	µg	13.8	2.1
Iodine	µg	83	12.5
Vitamins			
Vitamin A	µg RE (IU)	392(1305)	58.8(196)
Vitamin D	µg (IU)	8.7(348)	1.3(52.2)
Vitamin E	mg α-TE (IU)	4.6(6.9)	0.69/(1)
Vitamin K	µg	37.2	5.6
Thiamin	mg	0.5	0.08
Riboflavin	mg	0.5	0.08
Niacin	mg α-TE (IU)	2.2 (9)	0.33(1.4)
Pantothenic acid	mg	2.8	0.42
Vitamin B6	mg	0.5	7.4
Folic acid	µg	55	8.3
Vitamin B12	µg	1.2	0.18
Biotin	µg	18.2	2.7
Vitamin C	mg	49	7.4
Others			
Choline	mg	91	13.7
Myo-inositol	mg	98	14.7
Water			
Osmolality	mOsm/kg H_2O	-	380
Amino acid profile			
L-Alanine	g	1.6	0.24
L-Arginine	g	1.4	0.21
L-Aspartate Acid	g	1.27	0.19
L-Cystine	g	0.51	0.08
Glycine	g	0.64	0.1
L-Glutamine	g	0.11	0.02
L-Histamine	g	0.94	0.14

L-Isoleucine	g	<0.045	<0.007
L-Leucine	g	2.12	0.32
L-Lysine	g	1.43	0.21
L-Methionine	g	Nil added	Nil added
L-Phenylalanine	g	0.93	0.14
L-Proline	g	0.64	0.1
L-Serine	g	0.89	0.13
L-Threonine	g	Nil added	Nil added
L-Tryptophan	g	0.41	0.06
L-Tyrosine	g	0.93	0.14
L-Valine	g	Nil added	Nil added
L-carnitine	g	0.01	0.002
Taurine	g	0.03	0.005

XMTVI MAXAMAID			
Average contents	**Unit**	**per 100g**	**per 100ml 1 in 5 dilution**
Energy	Kcal	309	61.8
	kJ	1311	262.2
Protein (amino acids)	g(g)	25(30)	5(6)
Carbohydrate	g	51	10.2
Sugars	g	4.6	0.92
Lactose	g	-	-
Fat	g	<0.5	<0.1
Saturates	g	trace	Trace
Monosturates	g	trace	Trace
Polyunsaturates	g	trace	Trace
Dietary fibre	g	Nil added	Nil added
Minerals			
Sodium	mg(mmol)	580 (25.2)	116(5.1)
Potassium	mg(mmol)	840 (21.5)	168(4.3)
Chloride	mg(mmol)	450 (12.7)	90(2.5)
Calcium	mg(mmol)	810 (26.1)	162(4.1)
Phosphorus	mg(mmol)	810 (26.1)	162(4.1)
Magnesium	mg(mmol)	200 (8.3)	40(1.7)
Iron	mg	12	2.4
Zinc	mg	13	2.6
Copper	µg	1800	360
Manganese	mg	1.6	0.32
Fluoride	mg	-	-
Molybdenum	µg	100	20
Selenium	µg	40	8
Chromium	µg	40	8
Iodine	µg	100	20
Vitamins			

Vitamin A	µg RE (IU)	525(1748)	105(349.6)
Vitamin D	µg (IU)	12 (480)	2.4(96)
Vitamin E	mg α-TE (IU)	4.35 (6.5)	0.87(1.3)
Vitamin K	µg	30	6
Thiamin	mg	1.08	0.216
Riboflavin	mg	1.2	0.24
Niacin	mg α-TE (IU)	12 (25.5)	2.4(5.1)
Pantothenic acid	mg	3.7	0.74
Vitamin B6	mg	1.4	0.28
Folic acid	µg	240	48
Vitamin B12	µg	3.9	0.78
Biotin	µg	120	24
Vitamin C	mg	135	27
Others			
Choline	mg	110	22
Myo-inositol	mg	55.5	11.1
Water			
Osmolality	mOsm/kg H_2O	-	690
Amino acid profile			
L-Alanine	g	3.05	0.61
L-Arginine	g	2.71	0.542
L-Aspartate Acid	g	2.41	0.482
L-Cystine	g	1	0.2
Glycine	g	1.22	0.244
L-Glutamine	g	0.33	0.066
L-Histamine	g	1.83	0.366
L-Isoleucine	g	<0.075	<0.015
L-Leucine	g	4.11	0.822
L-Lysine	g	2.8	0.56
L-Methionine	g	Nil added	Nil added
L-Phenylalanine	g	1.81	0.362
L-Proline	g	1.22	0.244
L-Serine	g	1.71	0.364
L-Threonine	g	Nil added	Nil added
L-Tryptophan	g	0.81	0.162
L-Tyrosine	g	1.82	0.364
L-Valine	g	Nil added	Nil added
L-carnitine	g	0.02	0.004
Taurine	g	0.1	0.02

Table 4: Serving lists for protein – restricted diets: Approximate nutrient content per serving

Food list	Nutrient					
	ILE (mg)	MET (mg)	THR (mg)	VAL (mg)	Protein (g)	Energy (kcal)
Breads/Cereals	25	10	25	35	0.70	30
Fats	5	2	5	5	0.10	30
Fruits	10	5	10	15	0.50	55
Vegetables	15	5	15	20	0.50	10

Table 5: Natural protein analysis

	Leucin (mg)	Isoleucine (mg)	Methionine (mg)	Tryptophan (mg)	Phenylalanine (mg)	Threonine (mg)	Lysine (mg)	Valine (mg)	Protein (mg)	Energy (mg)
Human milk 30 ml	**21**	**17**	**6**	**5**	**14**	**14**	**21**	**19**	**-**	**-**
Soybean milk 240 ml	802	460	142	134	513	463	708	489	-	-
Whole milk 1 ml	**3.29**	**2.03**	**0.85**	**0.47**	**1.62**	**1.52**	**2.66**	**2.24**	**0.0336**	**0.62**
Low fat milk 1 ml	3.2	2	0.009	0.41	1.6	1.5	2.6	2.2	0.03	0.7
Skimmed milk 1 ml	3.34	2.06	0.86	0.48	1.65	1.54	2.7	2.28	0.034	0.35
Nido/whole milk powder 1 gm	25.7	15.9	6.5	3.9	12.7	11.8	20.8	17.6	0.26	4.9
Skimmed milk powder 1 gm	35.4	21.8	9	5.1	17.4	16.3	28.6	24.2	0.36	3.6
Whole yogurt plan 1ml	3.3	1.79	0.96	0.18	1.79	1.34	2.9	2.7	0.03	0.6
Low fat yogurt plan 1 ml	5	2.7	1.46	0.27	2.7	2.03	4.45	4.1	0.05	0.6
Skim yogurt plan 1 ml	5.4	2.9	1.59	0.3	2.9	2.2	4.8	4.4	0.05	0.5
Isomil 1 gm powder	10.75	5.78	3.19	1.63	6.75	4.93	7.54	5.82	0.137	5.17
Similac 1 gm powder	**10.32**	**5.36**	**2.71**	**1.51**	**4.6**	**5.53**	**8.4**	**5.7**	**0.118**	**5.26**
Pediasure 1 ml	**2.776**	**1.48**	**0.804**	**-**	**-**	**1.34**	**-**	**1.764**	**0.03**	**1**
Whole egg 50 gm	533	380	196	97	343	298	4.1	4.37	6.07	79
Cream cheese 20 gm	207	113	51	19	119	91	192	125	2.1	99
Coconut fresh shredded ½ cup	130	87	34	16	48	62	73	103	-	-
Peanut butter 1 tbs	272	148	39	0	227	120	160	223	-	-
Lentil cooked 2/2 cup 100 gm	554	413	55	10	359	273	476	421	-	-
Thyme (za'atar)	6	7	0	3	0	4	3	7	-	-
Mustard	59	36	16	17	35	36	50	44	-	-
Sesame seeds 23 gm	443	250	168	87	387	188	153	234	-	-
Fenugreek seed 1 tebs/4 gm	65	45	13	14	40	33	62	41	-	-
Farina rice cereal 1 cup / 100 gm	1130	690	260	180	475	645	945	720	-	-
Corn flour 110 gm / 1 cup	1118	396	163	52	387	344	249	139	-	-
Rice flour 125 gm / 1 cup	645	352	135	82	375	292	292	525	-	-
All-purpose flour 11 tbs	719	364	186	129	526	285	235	432	10.5	365
20 tbs cocoa – no milk or sugar	372	241	61	100	303	241	317	363	18	280
Potato chips 20 gm	55	48	13	11	48	45	58	58	1.1	113

Chapter 3

Nutrition Support for Maple Syrup Urine Disease (MSUD)

Introduction:

Maple Syrup Urine Disease (MSUD), is an inherited disorder in which the body is unable to process certain protein building blocks (branched chain amino acids, BCAA) properly. The condition gets its name from the distinctive sweet odor of affected infants' urine. MSUD occur when the branched-chain alpha-keto acid dehydrogenase (BCKAD) activity is deficient. BCKAD is essential for breaking down the amino acids leucine, isoleucine, and valine (BCAA).

Clinical Features:

There are several variations of the disease and these overlapping:

- Classic Severe MSUD
- Intermediate MSUD
- Intermittent MSUD
- Thiamine-responsive MSUD
- E3-Deficient MSUD with Lactic Acidosis

The most common and severe form of the disease is the classic type, which appears soon after birth, and as long as it

remains untreated, it gives rise to progressive and unremitting symptoms. Variant forms of the disorder may appear later in infancy or childhood, with typically less severe symptoms that may only appear during times of fasting, stress or illness, but still involve mental and physical problems if left untreated.

Typically the symptoms of classical form start in the first 3-4 days as poor feeding, irritability, deepening encephalopathy, which manifests as lethargy, intermittent apnea, opsithotonus and stereotyped abnormal movements, by seven to ten days, coma, cerebral edema and central respiratory failure may occur.

Patients with intermediate MSUD have partial BCKAD enzyme deficiency that only manifest intermittently, or respond to thiamine therapy; those individuals can experience severe metabolic decompensation and encephalopathy during catabolic stress e.g. illness.

Diagnosis:

MSUD can be diagnosed in presence of suggestive clinical features with elevated BCAAs and allo-isoleucine in plasma, and along with BCAAs metabolites in the urine.

Most of MSUD cases now diagnosed by newborn screening programs (NBS) using tandem Mass Spectrometry (T/MS), however tandem MS only measures the combined peak of leucine and isoleucline and their ratio to other amino acids such alanine and phenylalanine.

Quantitative Plasma Amino Acid (PAA) can measure all BCAA with allo-isoleucine, which are needed for acute management and monitoring.

Genetic Counseling:

The MSUD is inherited as autosomal recessive manner, at conception; the mother of affected proband has 25% chance of having another affected child.

Mutations in the following genes can cause maple syrup urine disease:

- BCKDHA, encoding BCKA decarboxylase (E1) alpha subunit
- BCKDHB, encoding BCKA decarboxylase (E1) beta subunit
- DBT, encoding dihydrolipoyl transacylase (E2) subunit
- DLD, encoding dihydrolipoamide dehydrogenase (E3) subunit.

Carrier testing and prenatal diagnosis is possible if the pathogenic mutation in the family is known.

Management:

Decompensation caused by catabolic stress (e.g. vomiting, diarrhea, febrile illness and decreased oral intake) management MSUD can be classified as

- **Acute Management**
- **Chronic management**

Acute Management: acute severe catabolism with encephalopathy patients need to be managed immediately and aggressively using administration of high caloric intake (IVF 10% Dextrose and IV lipids). Keeping patients NPO for 12-24 hours and may be more, lead to restriction of protein to reduce the BCAA amount in the diet. Careful measurement of BCAA during acute management and valine and isoleucine supplementation may be needed to bring down the leucine to target level.

In case of encephalopathy and severe elevation of leucine >1500 µmol/L hemodialysis (CRRT) should be considered for rapid decrease of toxic leucine and its metabolites from extracellular compartment. Brain edema is a common complication of metabolic decompensation and requires careful management in an ICU setting.

Chronic Management: long term management and monitoring is always needed to prevent catabolism during illness. To prevent further neurological manifestations by dietary restriction of protein, use of special formulas and sick days recipe. Careful and frequent monitoring of BCAA, to keep them at target therapeutic level, is essential part of MSUD management.

Nutritional Support for Maple Syrup Urine Disease (MSUD)

Rational for nutritional support:

- To restrict dietary BCAAs (ILE, LEU, and VAL) to amount tolerated by patients, to maintain plasma amino acid concentration within normal range (Table 1).
- Maintain normal growth and development.

Long term nutritional support:

1. ILE, LEU and VAL requirements (table 2)
   a) Requirements vary widely from patient to patient and in the same patient depending on age, growth rate, adequacy of energy and protein intake and state of health.
   b) Changing requirements of patients are determined by frequent monitoring of:
      - Plasma ILE, LEU, and VAL concentrations.
      - Urine concentrations of Branched-Chain α-Ketoacids.

With ILE, LEU, and VAL concentrations in normal range, plasma amino acids must be measured frequently to prevent deficiency.

2. Protein:
   a) Prescribe protein intake greater than RDA. (Table 2)
   b) Adequate protein intake that supports normal growth result in greater tolerance to restricted BCAAs.
3. Energy:
   a) Prescribe amount that should support normal weight gain in infants and children and maintain appropriate weight for height in adults. (Table 2)
   b) At diagnosis and during metabolic acidosis resulting from infection, energy needs may be 25% to 40% higher than requirement.
   c) Inadequate energy intake may result in depressed tolerance of BCAAs and increased concentrations of plasma BCAAs.
4. Fluid:

   Prescribe amount that will supply water requirements. (Table 2) Normally offer minimum of 1.5ml fluid to neonates and 1.0ml to children and adults for each kcal ingested.

Initiation of nutritional management during critical illness:

- Initiate nutritional support immediately, don't wait for confirmation of diagnosis.
- Evaluate plasma concentration of ILE, LEU, and VAL daily.
- Depending on clinical status, feed patient per oral or nasogastric tube; begin high-energy feeds (120-150

kcal/kg for infants, 80-100 kcal/kg for children) with adequate water. (Table 2)

- Introduce MSUD Anamix infant (nutricia) or ketonex-1 (Abbot).
- (Table 3 &4)
- Add ILE & VAL supplement to the synthetic protein when plasma concentration reach upper limit of treatment range, (Table 5) usually within 1-4 days of starting nutritional support (as per protocol).

NOTE:

1. **Plasma LEU concentration will NOT decrease to normal range if intake of either ILE or VAL is deficient.**
2. **Patients will develop severe skin and eye lesions if ILE deficiency occurs.**

- Add LEU to MSUD Anamex infant/Ketonex-1 feeds.
    - when plasma LEU concentration reaches upper limit of treatment range (within 7-10 days) (Table 5)
    - Use infant formula or whole cow's milk (Table 6) depending on age, to fill LEU prescription.

LEU, the last amino acid to become normal in plasma, remains elevated for prolonged period, if ILE and/or VAL are deficient

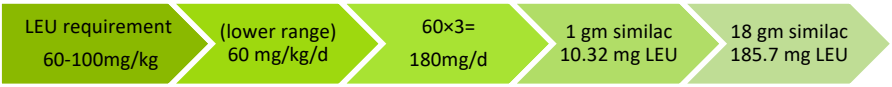
- Determine amounts of ILE and VAL in infant formula or whole cow's milk required to supply LEU.
- Decrease (adjust) volumes of ILE and VAL supplementation added to the synthetic protein in

the begging by amount of ILE and VAL supplied by infant formula or whole cow's milk.

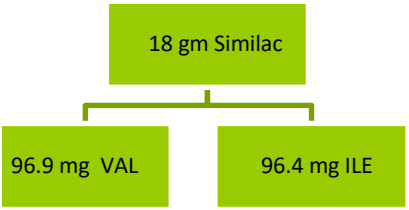
- Weigh powdered infant formula on scale that reads in grams.

Example: (for 3kg infant)

- LEU:
  1. Calculate amount of infant formula whole cow's milk, or table foods required to fill LEU prescription (Tables 2,6,7)



  2. Parents may select any food in prescribed food lists (Table 7) in specified amounts to fill LEU prescription.
  3. ILE and VAL :
     a) Calculate approximate amounts of ILE and VAL provided by infant formula, whole cow's milk, or table foods.



     b) Subtract amount determined above from total ILE and VAL prescriptions.

From Requirement:

VAL 42-70 mg/kg	ILE 36-60 mg/kg
(126 mg/d)	(108 mg/d)
126-96.9 = 30mg	108-96.4 = 12mg

c) Supply any remaining prescribed ILE and VAL as individual solution supplement of:

VAL : 30 mg/d

ILE: 12 mg/d

d) If plasma concentrations of ILE and VAL are in normal range, supplementation are not required

4. Protein :

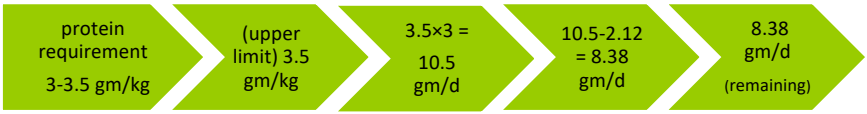
a) Calculate amount provided by infant formula, whole cow's milk or table foods required to fill LEU, ILE, and VAL (Tables 6,7)

Similac 18gm

2.12 gm protein/d

b) Subtract the amount determined from the total protein prescription

Protein Requirement:



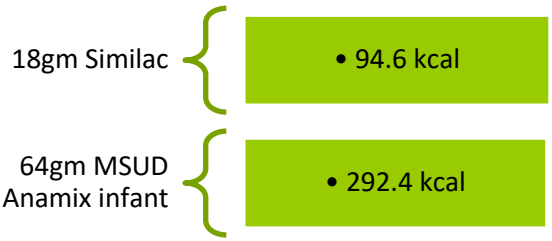
c) Supply any remaining prescribed protein with
   - MSUD Anamix infant (nutricia) or ketonex-1 (Abbot) for infants and toddlers.

1gm MSUD Anamix infant = 0.131gm protein

64gm MSUD Anamix infant= 8.38gm protein

   - MSUD Anamix Junior (nutricia) or ketonex-2 (Abbot) for children and adults

5. Energy :
   a) Calculate energy provided by synthetic and natural protein required to fill LEU, ILE, VAL and protein prescriptions.



b) Subtract the amount from total energy prescription

c) Provide any reaming prescribed energy with Polycose (3.8 kcal/gm) or Prophree (5.2 kcal/gm), if needed.

6. Fluid:
   a) Add sufficient water to infant formula, synthetic protein and the energy supplement and mix in sterilized, tightly closed container by shaking for 10 to 12 seconds.
   b) Refrigerate in sterilized, closed containers until used. discard unused formula after 24 hours.
   c) Provide parents, caregiver with completed Diet Guide.
   d) Feed young infants 6-8 times daily, feed children and adults 4-6 times daily.

Evaluation and Monitoring

1. Plasma BCAAs:

   Evaluate daily until plasma concentration stabilized and approximate BCAA requirements are known

2. Unacceptable amino acid concentrations:

If plasma ILE, LEU, or VAL is not detected and patient has ingested full formula, increase prescribed amount of undetected amino acid(s) by 5-10% and reevaluate plasma concentration in 3 days, repeat until value is in treatment range.

3. Urine Ketoacids by Ketostix
    - Evaluate once daily to 6 months of age and twice weekly thereafter.
    - If patient is ill, evaluate daily.
    - Urine should be free of ketoacid at all times.
    - If urine contain ketoacids, immediately obtain plasma LEU.
4. Growth status:
    - Monitor weight and height with every clinic visit and must be plot on NCHS growth charts
    - If patient remains below usual growth channel and does not respond to increase in protein and energy or cannot consume diet prescribed through oral feeding, nasogastric or gastrostomy tube feeding should be considered
    - Maintain records of food intake for 3 days immediately before each blood test
    - Evaluate intake of BCAAs, protein, and energy before and after each blood test. (Tables 7,8)

Example:

New born baby boy with MSUD weigh: 3.3 kg

Nutrients Requirements: **Give**

- Energy 120-145 kcal/kg 390 kcal/d
- Protein 3- 3-.5 gm/kg 10.5 gm/d
- Valine 42- 70 mg/kg 126 mg/d
- Isoleucine 36-60 mg/kg 108 mg/d
- Iucinen 60-100 mg/kg 180 mg/d

100% N.P	Amount gm	Iucine mg	Valine mg	Isolucine mg	Protein		Energy Kcal
					N.P. gm	AA gm	
Similac	18	165.7	96.9	96.4	2.12		94.68
MSUD Anamix infant	64					8.38	292.4
Supplement			30 mg	12 mg			
Total /d					10.5		387.2
Total /kg					3.5		129

Add 450 ml water to reach total volume 500ml and the feed will be 60-70cc q3 hrs. (24 kcal/oz)

50% N.P	Amount gm	Iucine mg	Valine mg	Isolucine mg	Protein		Energy Kcal
					N.P. gm	AA gm	
Similac	9				1.6		47.3
MSUD Anamix infant	72					9.43	329
Total \d					10.49		376
Total \kg					3.49		125.4

Add 420 ml water to reach total volume 470ml and the feed will be 60-70cc q3 hrs. (24 kcal/oz)

Table 1: Normal target amino acids references by age:

Recommended daily nutrient intakes of BCAA, PRO, energy and fluids for individuals with MSUD when well.[a]

Age	Nutrient					
	LEU mg/kg	ILE mg/kg	VAL mg/kg	Protein g/kg	Energy kcal/kg	Fluid mL/kg
0 to 6 months	40–100	30–90	40–95	2.5–3.5	95–145	125–160
7 to 12 months	40–75	30–70	30–80	2.5–3.0	80–135	125–145
1–3 years	40–70	20–70	30–70	1.5–2.5	80–130	115–135
4–8 years	35–65	20–30	30–50	1.3–2.0	50–120	90–115
9–13 years	30–60	20–30	25–40	1.2–1.8	40–90	70–90
14–18 years	15–50	10–30	15–30	1.2–1.8	35–70	40–60
19 years +[b]	15–50	10–30	15–30	1.1–1.7	35–45	40–50

[a] Adapted from Marriage, B [21].
[b] Males and non-pregnant, non-lactating females.

Table 2: Recommended daily nutrient intakes (range) for infants, children and adults MSUD

Amino Acid	**(2-4 hrs. postprandial)**			
	Newborn	1-3 m	3m-6y	6-18y
LEU	61-183	43-165	40-158	79-174
ILE	27-80	32-87	13-81	38-95
VAL	78-264	96-291	85-334	156-288
GLU	243-822		475-746	360-740
ALA	132-455	134-416	148-475	193-545

Table 3: Nutrient composition of Ketonex-1 and Ketonex -2

Nutrient	Cyclinex-1		Cyclinex-2	
	(per 100 g pwd)	(per g protein equiv)	(per 100 g pwd)	(per g protein equiv)
Energy, kcal	480	32	410	13.7
Protein equiv, g	15.00	1.000	30.00	1.000
Nitrogen, g	2.40	0.160	4.8	0.160
Amino acids, g	14.45	0.963	28.90	0.963
Cystine, g	0.15	0.010	0.30	0.010
Histidine, g	0.42	0.28	0.84	0.028
Isoleucine, g	Trace	0.000	Trace	0.000
Leucine, g	Trace	0.000	Trace	0.000
Lysine, g	1.00	0.067	2.00	0.067
Methionine, g	0.30	0.020	0.60	0.020
Phenylalanine, g	0.88	0.059	1.76	0.059
Threonine, g	0.70	0.049	1.40	0.047
Tryptophan, g	0.17	0.011	0.34	0.011
Tyrosine, g	0.89	0.059	1.78	0.059
Valine, g	trace	0.000	Trace	0.000
Other Nitrogen-Containing Compounds				
L-Carnitine, mg	100	6.67	200	6.67
Taurine, mg	40	2.67	50	1.67
Carbohydrate, g	53.0	3.53	35	1.17
Fat, g	21.7	1.45	14	0.47
Linoleic acid, g	2.00[4]	0.133	1.50[6]	0.050
α-Linoleic acid, g	0.36[5]	0.024	0.17[7]	0.006
Minerals				
Calcium, mg	575	38	880	29
Chloride, mg/mEq	325/9.17	21.7/0.61	940/26.51	31.33/0.88
Chromium, µg	11	0.73	27	0.90
Copper, mg	1.10	0.073	1.00	0.033
Iodine, µg	65	4.33	100	3.33
Iron, mg	9.0	0.60	13	0.43
Magnesium, mg	50	3,33	225	7.50
Manganese, mg	0.50	0.033	0.80	0.027
Molybdenum, µg	12	0.80	30	1.00
Phosphorus, mg	400	27	760	25
Potassium, mg/mEq	675/17.26	45/1.15	1,370/35.04	45.7/1.17
Selenium, µg	20	1.33	35	1.17
Sodium, mg/mEq	190/8.26	12.7/0.55	880/38.28	29.3/1.28
Zinc, mg	8.0	0.53	13	0.43

Vitamins				
A, µg RE	420	28	660	22
D, µg	7.50	0.50	7.50	0.25
E, mg α-TE	10.10	0.67	12.10	0.40
K, µg	50	3.33	60	2.00
Ascorbic acid, mg	50	3.33	60	2.00
Biotin, µg	65	4.33	100	3.33
B_6, mg	0.75	0.050	1.30	0.043
B_{12}, µg	4.90	0.327	5.00	0.167
Choline, mg	80	5.33	100	3.33
Folate, µg	230	15	450	15
Inositol, mg	40	2.67	70	2.33
Niacin equiv, mg	12.80	0.850	21.7	0.72
Pantothenic acid, mg	6.90	0.460	8.00	0.267
Riboflavin, mg	0.90	0.060	1.80	0.060
Thiamin, mg	1.90	0.127	3.25	0.108

Table 4: Nutrient composition of MSUD Anamix Infant and MSUD Anamix Junior

MSUD ANAMIX INFANT			
Average contents	**Unit**	**per 100g**	**per 100ml***
Energy	Kcal	457	69
	kJ	1915	287
Protein (amino acids)	g(g)	13.1(15.5)	2(2.3)
Carbohydrate	g	49.5	7.4
Sugars	g	7.4	1.1
Lactose	g	1.6	0.24
Fat	g	23	3.5
Saturates	g	7.5	1.1
Monosturates	g	9.4	1.4
Polyunsaturates	g	5	0.8
DHA	g	0.07	0.01
LCT	%	97	-
LA/ALA	ratio	6.3:1	-
% energy linoleic acid	%	8.1	-
% energy linoleic α-acid	%	1.3	-
Dietary fibre	g	5.3	0.8
Minerals			
Sodium	mg(mmol)	191(8.3)	28.7(1.2)
Potassium	mg(mmol)	501(12.8)	75.2(1.9)
Chloride	mg(mmol)	355(10.1)	53.3(1.5)
Calcium	mg(mmol)	410(10.3)	61.5(1.5)
Phosphorus	mg(mmol)	300(9.7)	45(1.5)
Magnesium	mg(mmol)	58(2.4)	8.7(0.4)
Iron	mg	8.1	1.2
Zinc	mg	5.7	0.86
Copper	µg	430	64.5
Manganese	mg	0.43	0.06
Fluoride	mg	-	-
Molybdenum	µg	12	1.8
Selenium	µg	15.5	2.3
Chromium	µg	13.8	2.1
Iodine	µg	83	12.5
Vitamins			
Vitamin A	µg RE (IU)	392(1305)	58.8(196)
Vitamin D	µg (IU)	8.7(348)	1.3(52.2)
Vitamin E	mg α-TE (IU)	4.6(6.9)	0.69(1)
Vitamin K	µg	37.2	5.6

Thiamin	mg	0.5	0.08
Riboflavin	mg	0.5	0.08
Niacin	mg α-TE (IU)	2.2(9.2)	0.33(1.4)
Pantothenic acid	mg	2.8	0.42
Vitamin B6	mg	0.5	0.08
Folic acid	µg	55	8.3
Vitamin B12	µg	1.2	0.18
Biotin	µg	18.2	2.7
Vitamin C	mg	49	7.4
Others			
Choline	mg	91	13.7
Myo-inositol	mg	98	14.7
Water			
Osmolality	mOsm/kg H_2O	-	380
Amino acid profile			
L-Alanine	g	0.82	0.12
L-Arginine	g	1.4	0.21
L-Aspartate Acid	g	1.2	0.18
L-Cystine	g	0.52	0.08
Glycine	g	1.29	0.19
L-Glutamine	g	0.13	0.02
L-Histamine	g	0.8	0.12
L-Isoleucine	g	Nil added	Nil added
L-Leucine	g	Nil added	Nil added
L-Lysine	g	1.45	0.22
L-Methionine	g	0.34	0.05
L-Phenylalanine	g	0.94	0.14
L-Proline	g	1.56	0.23
L-Serine	g	0.96	0.14
L-Threonine	g	1.05	0.16
L-Tryptophan	g	0.42	0.06
L-Tyrosine	g	0.94	0.14
L-Valine	g	Nil added	Nil added
L-carnitine	g	0.01	0.002
Taurine	g	0.03	0.005

MSUD ANAMIX JUNIOR			
Average contents	**Unit**	**per 100g**	**per 100ml 1 in 5 dilution**
Energy	Kcal	390	113
	kJ	1639	474
Protein (amino acids)	g(g)	29(35)	8.4(10)
Carbohydrate	g	38	11
Sugars	g	3.8	1.1
Lactose	g	-	-
Fat	g	13.5	3.9
Saturates	g	1.5	0.44
Monosturates	g	8.4	2.4
Polyunsaturates	g	2.8	0.81
LCT	%	95	-
LA/ALA	ratio	-	-
% energy linoleic acid	%	5.3	-
% energy linoleic α-acid	%	1.4	-
Dietary fibre	g	Nil added	Nil added
Minerals			
Sodium	mg(mmol)	680(30)	197(8.7)
Potassium	mg(mmol)	980(25.1)	284(7.3)
Chloride	mg(mmol)	525(14.7)	152(4.4)
Calcium	mg(mmol)	945(23.6)	274(6.9)
Phosphorus	mg(mmol)	480(15.5)	139(4.5)
Magnesium	mg(mmol)	165(6.9)	47.9(2)
Iron	mg	14	4.1
Zinc	mg	10	2.9
Copper	µg	1100	320
Manganese	mg	0.8	0.23
Fluoride	mg	-	-
Molybdenum	µg	43	12.5
Selenium	µg	56	16.2
Chromium	µg	28	8.1
Iodine	µg	100	29
Vitamins			
Vitamin A	µg RE (IU)	570(1898)	165(550)
Vitamin D	µg (IU)	14(560)	4.1(162)
Vitamin E	mg α-TE (IU)	6(9)	1.72.6)
Vitamin K	µg	25	7.3
Thiamin	mg	0.93	0.27
Riboflavin	mg	1.1	0.32
Niacin	mg α-TE (IU)	15(30.8)	4.4(8.9)

Pantothenic acid	mg	3.9	1.1
Vitamin B6	mg	1.3	0.38
Folic acid	µg	100	29
Vitamin B12	µg	1.3	0.38
Biotin	µg	35	10.2
Vitamin C	mg	55	16
Others			
Choline	mg	80	23.2
Myo-inositol	mg	35	10.2
Water			
Osmolality	mOsm/kg H_2O	-	1130
Amino acid profile			
L-Alanine	g	1.82	0.53
L-Arginine	g	3.19	0.93
L-Aspartate Acid	g	2.66	0.77
L-Cystine	g	1.19	0.35
Glycine	g	2.84	0.82
L-Glutamine	g	3.92	1,14
L-Histamine	g	1.822	0.53
L-Isoleucine	g	Nil added	Nil added
L-Leucine	g	Nil added	Nil added
L-Lysine	g	3.3	0.96
L-Methionine	g	0.78	0.23
L-Phenylalanine	g	2.16	0.63
L-Proline	g	3.45	1
L-Serine	g	2.16	0.63
L-Threonine	g	2.4	0.7
L-Tryptophan	g	0.95	0.28
L-Tyrosine	g	2.16	0.63
L-Valine	g	Nil added	Nil added
L-carnitine	g	0.029	0.01
Taurine	g	0.216	0.06

Table 5: Treatment Ranges for Target Amino Acids in MSUD

Amino Acid	(2-4hr postprandial)
ALA	**150-500 umol/L**
GLUT	**400-800 umol/L**
ALLO	**0**
ILE	**150-300 umol/L**
LEU	**100- 250 umol/L**
VAL	**200-400 umol/L**

Table 6: Natural protein analysis

	Leucin (mg)	Isoleucine (mg)	Methionine (mg)	Tryptophan (mg)	Phenylalanine (mg)	Threonine (mg)	Lysine (mg)	Valine (mg)	Protein (mg)	Energy (mg)
Human milk 30 ml	**21**	**17**	**6**	**5**	**14**	**14**	**21**	**19**	**-**	**-**
Soybean milk 240 ml	802	460	142	134	513	463	708	489	-	-
Whole milk 1 ml	**3.29**	**2.03**	**0.85**	**0.47**	**1.62**	**1.52**	**2.66**	**2.24**	**0.0336**	**0.62**
Low fat milk 1 ml	3.2	2	0.009	0.41	1.6	1.5	2.6	2.2	0.03	0.7
Skimmed milk 1 ml	3.34	2.06	0.86	0.48	1.65	1.54	2.7	2.28	0.034	0.35
Nido/whole milk powder 1 gm	25.7	15.9	6.5	3.9	12.7	11.8	20.8	17.6	0.26	4.9
Skimmed milk powder 1 gm	35.4	21.8	9	5.1	17.4	16.3	28.6	24.2	0.36	3.6
Whole yogurt plan 1ml	3.3	1.79	0.96	0.18	1.79	1.34	2.9	2.7	0.03	0.6
Low fat yogurt plan 1 ml	5	2.7	1.46	0.27	2.7	2.03	4.45	4.1	0.05	0.6
Skim yogurt plan 1 ml	5.4	2.9	1.59	0.3	2.9	2.2	4.8	4.4	0.05	0.5
Isomil 1 gm powder	10.75	5.78	3.19	1.63	6.75	4.93	7.54	5.82	0.137	5.17
Similac 1 gm powder	**10.32**	**5.36**	**2.71**	**1.51**	**4.6**	**5.53**	**8.4**	**5.7**	**0.118**	**5.26**
Pediasure 1 ml	**2.776**	**1.48**	**0.804**	**-**	**-**	**1.34**	**-**	**1.764**	**0.03**	**1**
Whole egg 50 gm	533	380	196	97	343	298	4.1	4.37	6.07	79

Cream cheese 20 gm	207	113	51	19	119	91	192	125	2.1	99
Coconut fresh shredded ½ cup	130	87	34	16	48	62	73	103	-	-
Peanut butter 1 tbs	272	148	39	0	227	120	160	223	-	-
Lentil cooked 2/² cup 100 gm	554	413	55	10	359	273	476	421	-	-
Thyme (za'atar)	6	7	0	3	0	4	3	7	-	-
Mustard	59	36	16	17	35	36	50	44	-	-
Sesame seeds 23 gm	443	250	168	87	387	188	153	234	-	-
Fenugreek seed 1 tebs/4 gm	65	45	13	14	40	33	62	41	-	-
Farina rice cereal 1 cup / 100 gm	1130	690	260	180	475	645	945	720	-	-
Corn flour 110 gm / 1 cup	1118	396	163	52	387	344	249	139	-	-
Rice flour 125 gm / 1 cup	645	352	135	82	375	292	292	525	-	-
All-purpose flour 11 tbs	719	364	186	129	526	285	235	432	10.5	365
20 tbs cocoa – no milk or sugar	372	241	61	100	303	241	317	363	18	280
Potato chips 20 gm	55	48	13	11	48	45	58	58	1.1	113

Table 7: Serving lists for BCAA–restricted diets: Approximate Nutrient Content per Serving

Food list	Nutrient				
	ILE (mg)	LEU (mg)	VAL (mg)	Protein (g)	Energy (kcal)
Breads/Cereals	18	35	25	0.5	30
Fats	7	10	7	0.1	70
Fruits	17	25	22	0.6	75
Vegetables	22	30	24	0.6	15

Table 8: Weights and measures :Except for dry cereals and food dices, the following weights apply

Level	Level	
1 teaspoon(tsp)	1/3 Tbsp	4.8 g
1 tablespoon (Tbsp)	1/16th cup	14.3g
1/4 cup	4 Tbsp	57.2g
1/3 cup	5 Tbsp	76.2 g
1/2 cup	8 Tbsp	114.3g
2/3 cup	10 Tbsp	152.5g
3/4cup	12 Tbsp	171.5g
1 cup	16 Tbsp	228.6 g

Chapter 4

Nutritional Support for Mitochondrial Fatty Acid Oxidation Defects

Introduction:

A large group of inherited genetic disorders that result from an inability of the body to produce or utilize the enzymes that are required to oxidize fatty acids. The enzyme can be missing or improperly constructed, nonfunctioning. This leaves the body unable to produce energy within the liver and muscles from fatty acid sources.

The primary source of energy in our body is glucose; when all the glucose in the body has been consumed, a normal body starts to digest fats. Patients with fatty-acid oxidation defects are unable to metabolize this fat source for energy.

A number of enzymes are needed to break down fats in the body (a process called fatty acid oxidation). Problems with any of these enzymes can cause a fatty acid oxidation disorder.

Here is incomplete list of various fatty-acid metabolism disorders:

- Carnitine Transport Defect
- Carnitine-Acylcarnitine Translocase (CACT) Deficiency
- Carnitine Palmitoyl Transferase I & II (CPT I & II) Deficiency
- Electron Transfer Flavoprotein (ETF) Dehydrogenase Deficiency (GAII & MADD)
- Very long-chain acyl-coenzyme A dehydrogenase deficiency (VLCAD deficiency)
- Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency (LCHAD deficiency)
- Medium-chain acyl-coenzyme A dehydrogenase deficiency (MCAD deficiency)
- Short-chain acyl-coenzyme A dehydrogenase deficiency (SCAD deficiency)

Clinical Features:

The symptoms of FAOD disorders vary and depend on the type of fatty acid oxidation disorder. Individuals without treatment, may experience periods of poor feeding, lack of energy, difficulty in breathing (apnea), low blood glucose (sugar) and vomiting. These episodes can become serious enough to lead to developmental delay, seizures, coma and even sudden death.

Without effective treatment, subsequent symptoms may include:

- hepatic disease
- cardiomyopathy
- cardiac conduction defects (arrhythmia)
- peripheral neuropathy
- myopathy

Diagnosis:

Most of these disorders are usually diagnosed by newborn screening program (e.g. MCAD, VLCAD, LCHAD and CPT) using Tandem Mass Spectrometry (Tandem MS). Analysis of fatty acid beta-oxidation in cultured fibroblasts or enzyme activity in leukocytes, fibroblasts, liver, heart, or skeletal muscle can be used to confirm the diagnosis or by molecular genetic testing if it remains in question.

Genetic Counseling:

Fatty acid oxidation disorders are inherited in an autosomal recessive pattern. Most often, the parents of a child with an autosomal recessive condition are not affected because they are “carriers”, with one copy of the changed gene and one copy of the normal gene. When both parents are carriers, there is a one-in-four (or 25%) chance that both will pass a changed gene on to a child.

Carrier testing and prenatal diagnosis is possible if the pathogenic mutation in the family is known.

Management:

In Symptomatic patients, the most important aspect of treatment is to avoid progression of the disease and acute decompensations, which may be aggravated by illness, fasting and dehydration, by reversal of catabolism and sustained anabolism by provision of simple carbohydrates by mouth.

If the patient was hypoglycemic, IV administration of glucose should then be initiated immediately with a bolus of 2 ml/kg 25% dextrose, followed by 10% dextrose with appropriate electrolytes at a rate of 10-12 mg glucose/kg/minute and to achieve and maintain blood glucose level higher than 5 mmol/L.

In asymptomatic individuals the mainstay in the treatment of FAOD is avoidance of fasting. Infant formulas containing medium-chain triglycerides as the primary source of fat are needed except in MCAD.

Nutritional Support for Mitochondrial Fatty Acid Oxidation Defects

Outcome of nutritional support:

As with most metabolic disorders, severity of the enzyme defect, time of diagnosis, and long-term metabolic control influence the long-term outcome for these patients.

A diet restricted in long-chain-fatty acids but supplemented with MCT oil is the most effective treatment for infants and children affected with disorders of long-chain-FAO including decreased frequency of metabolic crises, improved muscle tone, sustained physical growth, and developmental gains.

Rational for nutritional support:

Restrict type and amount of dietary fat to level tolerated by patient and appropriate to diagnosis to decrease production of abnormal metabolites

Goals of nutrition support:

1. Support normal growth rate in infants and children, and maintain appropriate weight for height in adults.
2. Prevent EFA deficiency.
3. Support normal nutrition status: prevent catabolism and avoid prolonged fasting.
4. Avoid lipid storage in heart, liver and muscles.
5. Maintain adequate hydration.

Establish nutritional support: (All examples are for 3 kg infant)

1. Energy:

   Prescribe amount that support normal weight gain for infant and children, and maintain appropriate weight for height in adult. (Table 1)

   Energy :108 kcal /kg / d

   324 kcal/d

2. Protein :

   Prescribe amount that supplies 10-12% of total energy (Table 1) calculate grams of protein required

   Protein 2.2 gm/kg/d

   6.6 gm/d

Do not use skim milk before patient is 2 years old

3. Fat:

Very-long-chain and long-chain-FAO defects:

- Prescribe 30-40% of energy as fat

(30*324)/100= 97.2 kcal / 9 = 10.8gm

- Calculate grams of fat required
- Supply about 50-75% of fat energy with MCT oil (8.55 kcal/ml)

- **MCT oil 30% = (30*324)/100 = 97.2 kcal / 9 = 10.8gm**
- **LCT oil 10% = (10*324)/100 = 32.4kcal / 9 = 3.6gm**

- If formula/food fail to supply 3% of energy as linoleic acid and 1% as α-linolenic acid, add adequate amount of appropriate vegetable oil to supply.(Table-2)

Administer MCT oil ONLY if defect in long-chain-FAO is confirmed, MCT oil is harmful for patients with medium or short chain FAO defects.

4. Carbohydrate:
   - The reaming energy as carbohydrate.
   - Supply any remaining prescribed energy with POLYCOSE (3.8 kcal/gm) or table foods containing little or no fat.
5. Fluid:
   - Prescribe amount that will supply water requirements (Table 1). Normally offer minimum of 1.5ml fluid to neonates and 1.0ml to children and adults for each kcal ingested.

     Add sufficient water to infant formula and the energy supplement and mix in sterilized, tightly closed container by shaking for 10 to 12 seconds

5gm monogen = 25ml water

78gm monogen = 390ml water

Refrigerate in sterilized, closed containers until used discard unused formula after 24 hours.

Feed young infants 6-8 times daily, feed children and adults 4-6 times daily. Provide parents, caregiver with completed Diet Guide

Example : (New born baby 3 kg)

Nutrition Requirement (RDA)	Give
• Energy :108 kcal /kg / d	324 kcal/d
• Protein 2.2 gm /kg/d	6.6 gm/6

Fat :

- MCT oil 30% = (30*324)/100 = 97.2kcal / 9 = 10.8gm
- LCT oil 10% = (10*324)/100 = 32.4kcal / 9 = 3.6gm

Monogen:

100gm = 416kcal 78gm = 324 kcal	100gm = 11.1gm fat 78gm = 8. 58 gm fat	100gm = 12.5 gm protein 78gm = 9.75 gm protein	5gm = 25ml water 78gm = 390ml water

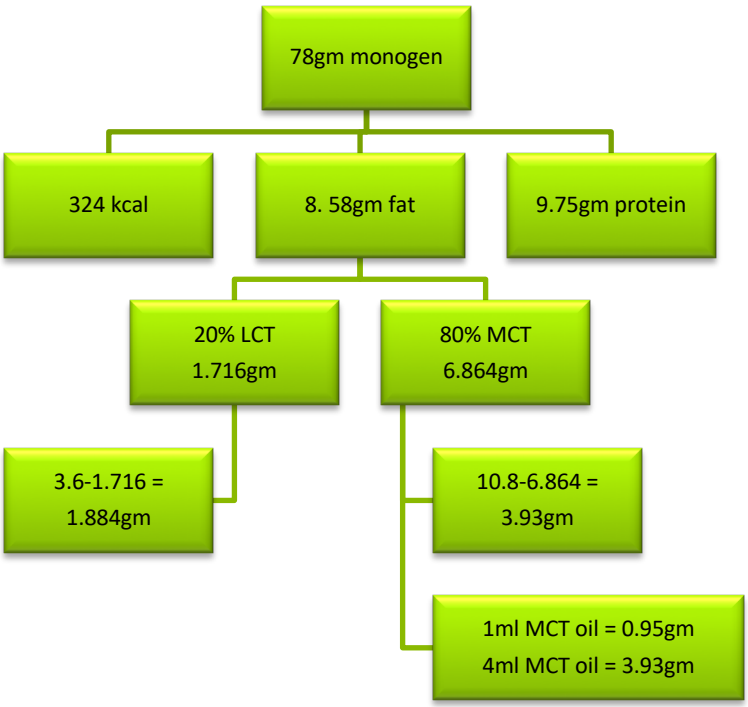


Table 1: Recommended daily nutrient intakes (Ranges) for infants, children and adults with a Mitochondrial FAO Defect

Age	Nutrient		
	Protein[1] (% of energy)	Energy[1] (kcal/kg)	Fluid[2] (mL/kg)
Infants			
0 to < 3 mo	10 - 12	120 (145 - 95)	150 - 125
3 to < 6 mo	10 - 12	115 (145 - 95)	160 - 130
6 to < 9 mo	10 - 12	110 (135 - 80)	145 - 125
9 to < 12 mo	10 - 12	105 (135 - 80)	135 - 120
	(g/day)	(kcal/day)	(mL/day)
Girls and Boys			
1 to < 4 yr	≥ 23	1,300 (900 - 1800)	900 - 1,800
4 to < 7 yr	≥ 30	1,700 (1300 - 2300)	1,300 - 2,300
7 to < 11 yr	≥ 34	2,400 (1650 - 3300)	1,650 - 3,300
Women			
11 to < 15 yr	≥ 46	2,200 (1500 - 3000)	1,500 - 3,000
15 to < 19 yr	≥ 46	2,100 (1200 - 3000)	1,200 - 3,000
≥ 19 yr	≥ 50	2,100 (1400 - 2500)	1,400 - 2,500
Men			
11 to < 15 yr	≥ 45	2,700 (2000 - 3700)	2,000 - 3,700
15 to < 19 yr	≥ 59	2,800 (2100 - 3900)	2,100 - 3,900
≥ 19 yr	≥ 63	2,900 (2000 - 3300)	2,000 - 3,300

Table 2: Sources of Essential Fatty Acid

Sources	Amount	Weight (g)	Total fat long chain (g)	Linoleic Acid (mg)	Linolenic Acid (mg)	Energy Kcal
Flax oil	1ml	0.9	0.9	114	480	8
Canola oil	1ml	0.9	0.9	183	84	8
Walnut oil	1ml	0.9	0.9	476	94	
Safflower oil	1ml	0.9	0.9	672	0	8
Corn oil	1ml	0.9	0.9	482	10	8
Soy oil	1ml	0.9	0.9	459	61	8
Sesame oil	1ml	0.9	0.9	372	3	8
Peanut oil	1ml	0.9	0.9	288	0	8
MCT oil	1ml	0.9	-	-	-	7.7
Margarine (soybean based)	1tsp	4.7	3 .78	1142	89	34
Mayonnaise (soybean based)	1tsp	5	3. 7	1700	193	44
Salad dressing (oil based)	1tsp	5	2 . 7	1200	75	24

Table 3: Exchange lists for nutritional support of children and Adults with Mitochondrial FAO Defect

Food	Measure	Fat (g)	Protein (g)	Energy (kcal)
Meat ,lean	1 OZ	3	7	55
Meat ,very lean	1 OZ	1	7	35
Milk ,skim	1 Cup	0.5	8	90
Fat	Varies	5	0	45
Fruit	½ cup canned or ½ cup fresh or Juice ½ cup dried	0	0	60 80
Starch /Bread	Varies	Trace	3	25
Vegetable	½ cup cooked ,or 1 cup raw	0.5	2	25

Table 4: Fat–Free food to help Supply Energy in low Fat diet

Food /Supplement	Measure	Energy
Carbonated beverages	4 floz	60
Corn syrup	1 Tbsp	57
Fruit and juice drinks	4 floz	60
Hard candy	3 pieces ,approx.	60
Jam,jelly	1 Tbsp	50
Jell-O	¼ cup , prepared	65
Polycose, glucose polymers	2 Tbsp	45
Popsicles , frozen juice bars	½ cup	50
Slush Drinks (ie, Mr. Misty)	1 floz	60
Syrup	1 Tbsp	55

Table 5: Nutrient composition of Monogen

MONOGEN			
Average contents	**Unit**	**per 100g**	**per 100ml***
Energy	Kcal	420	73.5
	kJ	1769	310
Protein (amino acids)	g(g)	12.5(2)	2.2(0.35)
Carbohydrate	g	68	12
Sugars	g	6.7	1.2
Lactose	g	0.7	1.9
Fat	g	11	1.9
Saturates	g	9.2	1.6
Monosturates	g	0.6	0.11
Polyunsaturates	g	0.6	0.11
% LCT	%	20	-
% MCT	%	80	-
N6:n3	ratio	6:2.1	-
% energy linoleic acid	%	1.1	-
% energy linoleic α-acid	%	0.17	-
Dietary fibre	g	-	-
Minerals			
Sodium	mg(mmol)	200(8.7)	35(1.5)
Potassium	mg(mmol)	360(9.2)	36(1.6)
Chloride	mg(mmol)	214(6)	37.5(1.1)
Calcium	mg(mmol)	257(6.4)	45(1.1)
Phosphorus	mg(mmol)	200(6.4)	35(1.1)
Magnesium	mg(mmol)	35(1.4)	6.1(0.25)
Iron	mg	4.2	0.74
Zinc	mg	3.3	0.58
Copper	µg	340	60
Manganese	mg	0.33	0.06
Fluoride	mg	-	-
Molybdenum	µg	21.4	3.7
Selenium	µg	10.8	1.9
Chromium	µg	10	1.8
Iodine	µg	40.6	7.1
Vitamins			
Vitamin A	µg RE (IU)	325(1082)	56.9(189)
Vitamin D	µg (IU)	6.6(264)	1.2(46.2)
Vitamin E	mg α-TE (IU)	2.75(4.1)	0.5(0.7)
Vitamin K	µg	21	3.7
Thiamin	mg	0.35	0.06
Riboflavin	mg	0.52	0.09

Niacin	mg α-TE (IU)	3.9(7.4)	0.68(1.3)
Pantothenic acid	mg	1.46	0.3
Vitamin B6	mg	0.4	0.07
Folic acid	µg	47	8.2
Vitamin B12	µg	0.86	0.2
Biotin	µg	22.3	3.9
Vitamin C	mg	35	6.2
Others			
Choline	mg	56	9.8
Myo-inositol	mg	85.7	15
Water			
Osmolality	mOsm/kg H_2O	-	280
Fatty acid profile			
C6	g	0.01	0.002
C8	g	4.77	0.83
C10	g	3.42	0.6
C12	g	0.08	0.01
C14:0	g	0.08	0.01
C16:0	g	0.53	0.09
C18:0	g	0.32	0.06
C18:1	g	0.53	0.09
C18:2	g	0.53	0.09
C18:3	g	0.08	0.01

Table 6: Nutrient composition of MCT Oil

MCT OIL		
Average contents	**Unit**	**per 100ml***
Energy	Kcal	855
	kJ	3515
Protein	g(g)	-
Carbohydrate	g	-
Fat	g	95
Saturates	g	95
Monosturates	g	-
Polyunsaturates	g	-
% MCT	%	100
Dietary fibre	g	-
Fatty acid profile		
C6	g	532
C8	g	45600
C10	g	30400
C12	g	152
C14:0	g	76

Chapter 5

Phenylketonuria (PKU)

Introduction:

Phenylketonuria (PKU) is an inborn error of metabolism involving impaired metabolism of the amino acid phenylalanine to tyrosine, that is caused by absent or virtually absent of phenylalanine hydroxylase (PAH) enzyme activity.

Phenylalanine hydroxylase (PAH) deficiency results in intolerance to the dietary intake of the essential amino acid phenylalanine (PHE) and produces a spectrum of disorders including

- Classical phenylketonuria (PKU),
- Non-PKU hyperphenylalaninemia (non-PKU HPA) and
- Variant PKU.

Classic PKU is caused by a complete or near-complete deficiency of phenylalanine hydroxylase activity; without dietary restriction of phenylalanine, most children with PKU develop profound and irreversible intellectual disability. Non-PKU HPA is associated with a much lower risk of impaired cognitive development.

Clinical Features:

PKU is commonly included in the newborn screening panel of most countries, with varied detection techniques. Most babies in developed countries are screened for PKU soon after birth, however in undiagnosed cases the disease may present clinically with microcephaly, epilepsy, severe intellectual disability, behavioral problems, hypopigmentation (excessively fair hair and skin) and a "musty odor" of the baby's sweat and urine (due to phenylacetate, a carboxylic acid produced by the oxidation of phenylketone). If PKU is untreated during the first months of life, the damage done to the brain is not reversible.

In general, individuals treated for PKU have good outcomes. Treated people may have no detectable physical, neurological, or developmental problems at all.

Diagnosis:

Most of PKU cases now diagnosed by newborn screening programs (NBS).

Quantitative Plasma Amino Acid (PAA) to measure Blood phenylalanine concentration and phenylalanine tolerance at the time of diagnosis to classify infants with hyperphenylalaninemia.

- Classical Phenylketonuria (PKU) is the most severe of the three types and in an untreated state is associated with plasma PHE concentrations greater than 1000 µmol/L and a dietary PHE tolerance of less than 500 mg/day.

- Non-PKU hyperphenylalaninemia (non-PKU HPA) is associated with plasma PHE concentrations consistently above normal (i.e. >120 µmol/L) but lower than 1000 µmol/L when an individual is on a normal diet.
- Variant PKU includes those individuals who do not fit the description for either PKU or non-PKU HPA

BH4 loading tests are done to determine which persons are BH4 responsive and which are not in order to relax or discontinue restriction of dietary phenylalanine in those who are responsive.

Genetic Counseling:

PKU are inherited in an autosomal recessive pattern. Mutations in the PAH gene cause phenylketonuria. Most often, the parents of a child with an autosomal recessive condition are not affected because they are "carriers", with one copy of the changed gene and one copy of the normal gene. When both parents are carriers, there is a one-in-four (or 25%) chance that both will pass a changed gene on to a child.

Carrier testing and prenatal diagnosis is possible if the pathogenic mutation in the family is known.

Treatment:

Treatment for affected individuals of all ages can be difficult and is enhanced with the teaching and support of multidisciplinary management care.

In classic PKU, A PHE-restricted diet and a PHE-free medical formula must be started as soon as possible after birth under the direction of a nutritionist. The target of treatment for the hyperphenylalaninemias is normalization of the concentrations of PHE and TYR (tyrosine) in the blood to prevent the cognitive deficits that are attributable to this disorder, PHE concentrations of 120-360 µmol/L (2-6 mg/dL) are generally regarded as safe.

For patients who have a positive BH4 loading test, supplementation with BH4 should be given (10-20 mg/kg daily in divided oral doses). Long-term treatment in responsive to BH4 has documented the maintenance of the phenylalanine-lowering effect.

Maternal PKU and pregnancy

If the Pregnant woman with PKU has high plasma PHE concentrations, her intrauterine environment will be hostile to a developing fetus as phenylalanine is a potent teratogen. It is strongly recommended that women with PKU use reliable methods of contraception to prevent unplanned pregnancies.

Women with PKU who are off diet and are planning a pregnancy should start a PHE-restricted diet prior to conception and should maintain plasma PHE concentrations between 120 and 360 µmol/L (2-6 mg/dL),

Nutritional support for Phenylketonuria (PKU)

Rational for nutritional support:

- Correct primary imbalance by restrict dietary PHE to amount tolerated by patient to maintain treatment plasma PHE concentration.
- Supplement dietary TYR as necessary to maintain normal plasma TYR concentration.
- Support normal growth rate in infant and children and maintain appropriate weight for height in adult
- Prevent catabolism

Calculation:

- **What to calculate:**
  1. PHE
     a) Prescribe PHE intake that promotes growth and development (Table 1).
     b) If diagnostic plasma PHE concentration is in higher range, delete PHE from diet (Table 2).
     c) When plasma PHE concentration reaches upper limit of treatment range (300 µmol/L), PHE must be added to the diet gradually as per (Table 3).
  2. TYR
     a) Prescribe TYR intake that maintains treatment plasma concentration (Table 1)

  3. Protein
     a) Prescribe amount greater than RDA (table-1)

4. Energy
    a) prescribe amount that should support normal weight gain in infants and children and maintain appropriate weight for height in adults (Table 1).
5. Fluid
    a) prescribe amount that will supply water requirement (Table 1).
    b) Offer 1.5 ml/kcal and 1.0 ml/kcal for neonates and children respectively.

- **How to calculate:**

1. nutrients requirements : (3.0 kg new born baby)

2. PHE
    a) Calculate amount of infant formula or table foods required to fill PHE prescription (Tables 4&5)

1gm Similac➔4.6mg PHE

21**0** ÷ 4.6 = 46gm Similac

    b) Measure infant formula on scale that reads in grams.

c) Add table food gradually to displace PHE provided by infant formula if the patient is developmentally ready

3. Protein

a) Calculate the amount of protein from the infant formula or food table that required to fill the PHE prescription

1gm Similac➔ 0.118gm protein

46gm Similac ➔ 5.4gm protein

b) Subtract amount determined above from total protein prescription

10.5gm – 5.4gm = 5.1gm protein remaining

Supply any remaining prescribed protein with Phenex-1

1gm Phenex-1 ➔ 0.15gm protein

5.1gm protein ➔ 34gm Phenex-1

c) Phenex-1 is for infant and toddlers and Phenex-2 is for children and adults (Table 6)

d) Measure Phenex powder by scale that reads in grams.

4. TYR
    a) Calculate amount of TYR provided by infant formula or table foods required to fill PHE prescription
    b) Calculate amount of TYR supplied by phenex required to fill protein prescription

> 1gm Phenex-1 ➔ 15mg TYR
>
> 510mg TYR ➔ 34gm Phenex-1

    c) Added together, values calculated above should fall within range of TYR requirement (Table 1)
    d) If not, supplement the remaining as pure suspension (only if plasma TYR is below normal)
5. Energy
    a) Calculate energy provided by infant formula or table foods and Phenex required to fill PHE and protein prescriptions

> 46gm Similac = 241.90 kcal
> 34gm Phenex-1 =163.2 kcal
> 241.90 + 163.2 = 405.1 kcal/day
> 405.1 kcal ÷ 3kg=135

    b) Subtract amount determined above from total energy prescription

c) Provide remaining prescribed energy with Ploycose (3.8 kcal/gm) or Prophree (5.2 kcal/gm) if needed.

6. Fluid :
   a) Add sufficient water to infant formula, synthetic protein and the energy supplement and mix in sterilized , tightly closed container by shaking for 10 to 12 seconds.
   b) Refrigerate in sterilized, closed containers until used. Discard unused formula after 24 hours.
   c) Provide parents, caregiver with completed Diet Guide.
   d) Feed young infants 6-8 times daily, feed children and adults 4-6 times daily.

Regular concentration 20 Kcal/oz

405 kcal = 530 ml water /day

Monitoring and Evaluation of nutrition support:

1. Plasma PHE and TYR concentration
   a) Initial, evaluate twice weekly until stabilize and approximate dietary PHE and TYR requirement are known.
   b) Ongoing frequent evaluation (monthly), help ensure adherence to nutrition support plan.

2. Unacceptable PHE concentrations:
    a) If >300 µmol/L, decrease PHE by 15mg from the prescribed PHE and reevaluate in 3 days.
    b) If continues >300 µmol/L, repeat above process until value is in treatment range.
    c) If <120 µmol/L, add 15mg to prescribed PHE and reevaluate plasma concentration in 3 days.

Protein status:

1. Evaluate pre-albumin every 3 months until patient is 1 year of age and every 6 months thereafter.
2. If pre-albumin is below standard, increase prescribed protein by 5-10% and reevaluate in 1 month (if plasma PHE is in treatment range, use Phenex to increase protein.

Growth status:

1. Monitor weight and height with every clinic visit and must be plot on NCHS growth charts.
2. If patient remains below usual growth channel and does not respond to increase in protein and energy or cannot consume diet prescribed through oral feeding, nasogastric or gastrostomy tube feeding should be considered.
3. Maintain records of food intake for 3 days immediately before each blood test.

Example:

New born baby with PKU weigh 3kg:

Nutrients Requirements:	Give:
• Energy: 95-145 kcal/kg	405kcal /day
• Protein: 3-3.5 gm/kg	10.5gm /day
• PHE: 25-70 gm/kg	210gm/day
• TYR: 300-350 gm/kg	1050gm/day

100% NP	Amount (gm)	PHE (mg)	TYR (mg)	Protein		Energy Kcal
				NP gm	AA gm	
Similac	46	211.6	-	5.4		241.90
Phenex-1	34		510		5.1	163.2
Total/d				10.5		405.1
Total /kg				3.5		135

Fluid: Add 530ml water

50 % NP	Amount (gm)	PHE (mg)	TYR (mg)	Protein		Energy Kcal
				NP gm	AA gm	
Similac	23	105.8		2.7		120.98
Phenex-1	52		780		7.8	249.6
Prophree	6					31
Total/d				10.5		401.58
Total /kg				3.5		134

Fluid :Add 530ml water

Table 1: Recommended daily Nutrient intakes (Ranges) for infants, children , and Adults with PKU

Age	Nutrient				
	PHE [1-3] (mg/kg)	TYR[1] (mg/kg)	Protein[4] (g/kg)	Energy[4] (kcal/kg)	Fluid[5] (mL/kg)
Infants					
0 to < 3 mo	25 - 70	300 - 350	3.50 - 3.00	120 (145 - 95)	160 - 135
3 to < 6 mo	20 - 45	300 - 350	3.50 - 3.00	120 (145 - 95)	160 - 130
6 to < 9 mo	15 - 35	250 - 300	3.00 - 2.50	110 (135 - 80)	145 - 125
9 to < 12 mo	10 - 35	250 - 300	3.00 - 2.50	105 (135 - 80)	135 - 120
	(mg/day)	(g/day)	(g/day)	(kcal/day)	(mL/day)
Girls and Boys					
1 to < 4 yr	200 - 400	1.72 - 3.00	≥ 30	1,300 (900 - 1800)	900 - 1,800
4 to < 7 yr	210 - 450	2.25 - 3.50	≥ 35	1,700 (1300 - 2300)	1,300 - 2,300
7 to < 11 yr	220 - 500	2.55 - 4.00	≥ 40	2,400 (1650 - 3300)	1,650 - 3,300
Women					
11 to < 15 yr	250 - 750	3.45 - 5.00	≥ 50	2,200 (1500 - 3000)	1,500 - 3,000
15 to < 19 yr	230 - 700	3.45 - 5.00	≥ 55	2,100 (1200 - 3000)	1,200 - 3,000
≥ 19 yr	220 - 700	3.75 - 5.00	≥ 60	2,100 (1400 - 2500)	2,100 - 2,500
Men					
11 to < 15 yr	225 - 900	3.38 - 5.50	≥ 55	2,700 (2000 - 3700)	2,000 - 3,700
15 to < 19 yr	295 - 1,100	4.42 - 6.50	≥ 65	2,800 (2100 - 3900)	2,100 - 3,900
≥ 19 yr	290 - 1,200	4.35 - 6.50	≥ 70	2,900 (2000 - 3300)	2,000 - 3,300

Table 2: Diagnostic plasma PHE + delete dietary PHE for (hours)

Diagnostic Plasma PHE		Delete Dietary PHE for
(µmol/L)	(mg/dL)	(Hours)
240 < 605	4 < 10	24
605 < 1210	10 < 20	48
1210 < 2420	20 < 40	72
≥2420	≥40	96

Table 3: Addition of PHE as per PHE plasma concentration

Plasma PHE		**Dietary PHE**
(µmol/L)	(mg/dL)	(mg/kg)
≤605	≤10	70
>605 to ≤1210	>10 to ≤20	55
>1210 to ≤1815	>20 to ≤ 30	45
>1815to ≤2420	>30 to ≤20	35
>2420	≥40	25

Table 4: Natural protein analysis

	Leucin (mg)	Isoleucin (mg)	Methionine (mg)	Tryptophan (mg)	Phenylalanine (mg)	Threonine (mg)	Lysine (mg)	Valine (mg)	Protein (gm)	Energy (kcal)
Human milk 30 ml	**21**	**17**	**6**	**5**	**14**	**14**	**21**	**19**	-	-
Soybeans milk 240 ml	802	460	142	134	513	463	708	489	-	-
Whole milk 1ml	**3.29**	**2.03**	**0.85**	**0.47**	**1.62**	**1.52**	**2.66**	**2.24**	**0.0336**	**0.62**
Low fat milk 1ml	3.2	2	0.009	0.41	1.6	1.5	2.6	2.2	0.03	0.7
Skimmed milk 1ml	3.34	2.06	0.86	0.48	1.65	1.54	2.7	2.28	0.034	0.35
Nido /whole milk powder 1gm	25.7	15.9	6.5	3.9	12.7	11.8	20.8	17.6	0.26	4.9
Skimmed milk powder 1gm	35.4	21.8	9	5.1	17.4	16.3	28.6	24.2	0.36	3.6
Whole yogurt plan 1ml	3.3	1.79	0.96	0.18	1.79	1.34	2.9	2.7	0.03	0.6
Low fat yogurt plan 1ml	5	2.7	1.46	0.27	2.7	2.03	4.45	4.1	0.05	0.6
Skim yogurt plan 1ml	5.4	2.9	1.59	0.3	2.9	2.2	4.8	4.4	0.05	0.5
Isomil 1gm powder	10.75	5.78	3.19	1.63	6.75	4.93	7.54	5.82	0.137	5.17
Similac 1gm powder	**10.32**	**5.36**	**2.71**	**1.51**	**4.6**	**5.53**	**8.4**	**5.7**	**0.118**	**5.26**
Pediasure 1 ml	**2.776**	**1.48**	**0.804**	-	-	**1.34**	-	**1.764**	**0.03**	**1**
Whole Egg 50 gm	533	380	196	97	343	298	4.1	4.37	6.07	79
Cream cheese 20 gm	207	113	51	19	119	91	192	125	2.1	99
Cocunt fresh shredded ½ cup	130	87	34	16	48	62	73	103	-	-
Peanuts butter 1Tbs	272	148	39	0	227	120	160	223	-	-
Lentil cooked 2/² cup 100gm	554	413	55	10	359	273	476	421	-	-
Thyme (za'atar)	6	7	0	3	0	4	3	7	-	-
Mustared	59	36	16	17	35	36	50	44	-	-
Sesame seeds 23 gm	443	250	168	87	387	188	153	234	-	-
Fenugreek seed 1Tebs/4gm	65	45	13	14	40	33	62	41	-	-
Farina Rice cereal 1 cup /100gm	1130	690	260	180	475	645	945	720	-	-
Corn flour 110gm /I cup	1118	396	163	52	387	344	249	139	-	-
Rice flour 125gm/1cup	645	352	135	82	375	292	292	525	-	-
All-purpose flour 11 Tbs	719	364	186	129	526	285	235	432	10.5	365
20 Tbs cocoa- No milk or sugar	372	241	61	100	303	241	314	363	18	280
Potato chips 20 gm	55	48	13	11	48	45	58	58	1.1	113

Table 5: Serving lists for PHE restricted diets: average nutrient content per serving

Food list	Nutrient			
	PHE (mg)	TYR (mg)	Protein (g)	Energy (kcal)
Breads/Cereals	30	20	0.6	30
Fats	5	4	0.1	60
Fruits	15	10	0.5	60
Vegetables	15	10	0.5	10

Table 6: Nutrient composition of Phenex-1 and Phenex-2

Nutrient	Phenex-1		Phenex-2, Unflavored		Phenex-2, Flavored	
	Per 100 g pwd	Per g protein equiv	Per 100 g pwd	Per g protein equiv	Per 100 g pwd	Per g protein equiv
Energy, kcal	480	32	410	13.7	410	13.7
Protein equiv, g	15.00	1.000	30	1.000	30	1.000
Nitrogen, g	2.40	0.160	4.80	0.160	4.80	0.160
Amino acids, g	15.79	1.053	31.58	1.053	31.58	1.053
Cystine, g	0.15	0.010	0.30	0.010	0.30	0.010
Histidine, g	0.42	0.028	0.84	0.028	0.84	0.028
Isoleucine, g	1.08	0.072	2.16	0.072	2.16	0.072
Leucine, g	1.68	0.112	3.36	0.112	3.36	0.112
Lysine, g	1.00	0.067	2.00	0.067	2.00	0.067
Methionine, g	0.30	0.020	0.60	0.020	0.60	0.020
Phenylalanine, g	Trace	-	Trace	0	Trace	0
Threonine, g	0.70	0.047	1.40	0.047	1.40	0.047

Tryptophan, g	0,17	0.011	0.34	0.011	0.34	0.011
Tyrosine, g	1.50	0.100	3.00	0.100	3.00	0.100
Valine, g	1.22	0.081	2.44	0.081	2.44	0.081
Other Nitrogen-Containing Compounds						
Carnitine, mg	20	1.33	40	1.33	40	1.33
Taurine, mg	40	2.67	50	1.67	50	1.67
Carbohydrate, g	53.0	3.53	35	1.17	36	1.20
Fat, g	21.7	1.45	14	0.47	13.5	0.45
Linoleic acid, g	2.00[4]	0.133	1.50[5]	0.050	1.50[5]	0.050
α-Linoleic acid, g	0.36[6]	0.024	0.17[7]	0.006	0.17[7]	0.006
Minerals						
Calcium, mg	575	38	880	29	880	29
Chloride, mg/mEq	325/ 9.17	21.7/0.61	940/26 .51	31.33/0. 88	940/26.51	31.33/ 0.88
Chromium, µg	11	0.73	27	0.90	27	0.90
Copper, mg	1.10	0.073	1.00	0.033	1.00	0.033
Iodine, µg	65	4.33	100	3.33	100	3.33
Iron, mg	9.0	0.60	13	0.43	13	0.43
Magnesium, mg	50	3.33	225	7.50	225	7.50
Manganese, mg	0.50	0.033	0.80	0.027	0.80	0.027
Molybdenum, µg	12	0.80	30	1.00	30	1.00
Phosphorus, mg	400	27	760	25	760	25
Potassium, mg/mEq	675/ 17.2 6	45/1.15	1,370/ 35.04	45.7/1.1 7	1,370/35. 04	45.7/1. 17
Selenium, µg	20	1.33	35	1.17	35	1.17
Sodium, mg/mEq	190/ 8.26	12.7/0.55	880/38 .28	29.3/1.2 8	880/38.28	29.3/1. 28
Zinc, mg	8.0	0.53	13	0.43	13	0.43
Vitamins						
A, µg RE	420	28	660	22	660	22
D, µg	7.50	0.50	7.50	0.25	7.50	0.25
E, mg α-TE	10.1 0	0.67	12.10	0.40	12.10	0.40
K, µg	50	3.33	60	2.00	60	2.00
Ascorbic acid, mg	50	3.33	60	2.00	60	2.00
Biotin, µg	65	4.33	100	3.333	100	3.333
B_6, mg	0.75	0.050	1.30	0.043	1.30	0.043
B_{12}, µg	4.90	0.327	5.00	0.167	5.00	0.167
Choline, mg	80	5.33	100	3.33	100	3.33
Folate, µg	230	15	450	15	450	15
Inositol, mg	40	2.67	70	2.33	70	2.33
Niacin equiv, mg	12.8 0	0.850	21.7	0.72	21.7	0.72

Pantothenic acid, mg	6.90	0.460	8.00	0.267	8.00	0.267
Riboflavin, mg	0.90	0.060	1.80	0.060	1.80	0.060
Thiamin, mg	1.90	0.127	3.25	0.108	3.25	0.108

Nutrient	Phenex-1		Phenex-2, Unflavored		Phenex-2, Flavored	
	Per 100 g pwd	Per g protein equiv	Per 100 g pwd	Per g protein equiv	Per 100 g pwd	Per g protein equiv
Energy, kcal	480	32	410	13.7		
Protein equiv, g	15.00	1.000	30.00	1.000		
Nitrogen, g	2.40	0.160	4.8	0.160		
Amino acids, g	14.45	0.963	28.90	0.963		
Cystine, g	0.15	0.010	0.30	0.010		
Histidine, g	0.42	0.28	0.84	0.028		
Isoleucine, g	Trace	0.000	Trace	0.000		
Leucine, g	Trace	0.000	Trace	0.000		
Lysine, g	1.00	0.067	2.00	0.067		
Methionine, g	0.30	0.020	0.60	0.020		
Phenylalanine, g	0.88	0.059	1.76	0.059		
Threonine, g	0.70	0.049	1.40	0.047		
Tryptophan, g	0.17	0.011	0.34	0.011		
Tyrosine, g	0.89	0.059	1.78	0.059		
Valine, g	trace	0.000	Trace	0.000		
Other Nitrogen-Containing Compounds						
L-Carnitine, mg	100	6.67	200	6.67		
Taurine, mg	40	2.67	50	1.67		
Carbohydrate, g	53.0	3.53	35	1.17		
Fat, g	21.7	1.45	14	0.47		
Linoleic acid, g	2.00[4]	0.133	1.50[6]	0.050		
α-Linoleic acid, g	0.36[5]	0.024	0.17[7]	0.006		
Minerals						
Calcium, mg	575	38	880	29		
Chloride, mg/mEq	325/9.17	21.7/0.61	940/26.51	31.33/0.88		
Chromium, µg	11	0.73	27	0.90		
Copper, mg	1.10	0.073	1.00	0.033		
Iodine, µg	65	4.33	100	3.33		
Iron, mg	9.0	0.60	13	0.43		
Magnesium, mg	50	3,33	225	7.50		
Manganese, mg	0.50	0.033	0.80	0.027		
Molybdenum, µg	12	0.80	30	1.00		
Phosphorus, mg	400	27	760	25		

Potassium, mg/mEq	675/17.26	45/1.15	1,370/35.04	45.7/1.17
Selenium, µg	20	1.33	35	1.17
Sodium, mg/mEq	190/8.26	12.7/0.55	880/38.28	29.3/1.28
Zinc, mg	8.0	0.53	13	0.43
Vitamins				
A, µg RE	420	28	660	22
D, µg	7.50	0.50	7.50	0.25
E, mg α-TE	10.10	0.67	12.10	0.40
K, µg	50	3.33	60	2.00
Ascorbic acid, mg	50	3.33	60	2.00
Biotin, µg	65	4.33	100	3.33
B_6, mg	0.75	0.050	1.30	0.043
B_{12}, µg	4.90	0.327	5.00	0.167
Choline, mg	80	5.33	100	3.33
Folate, µg	230	15	450	15
Inositol, mg	40	2.67	70	2.33
Niacin equiv, mg	12.80	0.850	21.7	0.72
Pantothenic acid, mg	6.90	0.460	8.00	0.267
Riboflavin, mg	0.90	0.060	1.80	0.060
Thiamin, mg	1.90	0.127	3.25	0.108

Chapter 6

Classical Homocystinuria

Introduction:

Homocystinuria is an inherited disorder in which the body is unable to process certain building blocks of proteins (amino acids) properly, which is caused by deficiency of cystathionine β-synthase (CBS), a pyridoxine (vitamin B6)-dependent enzyme. A block at CBS, limits transsulfuration and results in both increased homocysteine and increased methionine.

Clinical Features:

Two phenotypic variants are recognized:

- B6-responsive homocystinuria
- B6-non-responsive homocystinuria

B6-responsive homocystinuria is typically, but not always, milder than the non-responsive variant.

The clinical features of untreated homocystinuria due to CBS deficiency usually manifest in the first or second decade of life and include

- Developmental delay / intellectual disability
- Ectopia lentis (dislocation of the ocular lens) and/or severe myopia

- Skeletal abnormalities such as excessive height and limb length
- Vascular abnormalities characterized by thromboembolism
- Clinical suggestion of Marfan syndrome (although often joint flexibility is decreased in homocystinuria)

Diagnosis:

Classical Homocystinuria caused by CBS deficiency can be recognized by cardinal clinical and biochemical features of homocystinuria which are:

- Markedly increased concentrations of plasma homocystine, total homocysteine, homocysteine-cysteine mixed disulfide,
- Increased methionine level in Quantitative PAA
- Increased concentration of urine homocystine.

The Diagnosis of homocystinuria can be confirmed by detection of reduced cystathionine β-synthase (CBS) enzyme activity, or detection pathogenic variants in CBS, the gene encoding cystathionine β-synthase.

Pyridoxine (B6) challenge test:

The two phenotypic variants of classic homocystinuria; B6-responsive and B6-non-responsive homocystinuria have differing clinical description and management.

While continuing a normal diet, plasma is obtained for baseline measurements of amino acids, the affected individual is given 100 mg pyridoxine orally, and the

concentrations of plasma amino acids are again measured 24 hours later. A reduction of 30% or more in plasma homocystine or homocysteine and/or plasma methionine concentration suggests B6 responsiveness.

N.B. higher dosage of Pyridoxine (B6) can be given if no response but not more than 300 mg in infants.

Genetic Counseling:

Homocystinuria are inherited in an autosomal recessive pattern. Caused by mutations in the CBS, the gene encoding cystathionine β-synthase. Most often, the parents of a child with an autosomal recessive condition are not affected because they are "carriers", with one copy of the changed gene and one copy of the normal gene. When both parents are carriers, there is a one-in-four (or 25%) chance that both will pass a changed gene on to a child.

Carrier testing and prenatal diagnosis is possible if the pathogenic mutation in the family is known.

Treatment:

The principles of treatment are to correct the biochemical abnormalities, especially to control the elevated plasma homocystine and homocysteine and methionine concentrations to prevent further complications.

The best results occur in those individuals identified by newborn screening and treated shortly after birth in whom the plasma homocystine concentration is maintained below 100 μmol/L.

Dietary treatment:

- B6-non-responsive neonates require continuous strict methionine-restricted diet with frequent metabolic monitoring.
- The majority of B6-responsive individuals also require a protein-restricted diet for metabolic control.

Medications:

- Betaine: treatment with betaine provides an alternate remethylation pathway to convert excess homocysteine to methionine. Although the increase in methionine produced by betaine is usually harmless, but cerebral edema has occurred when hypermethioninemia is extreme (>1000 µmol/L)
- Folate and vitamin B12 supplementation: folate and vitamin B12 as cofactors optimize the conversion of homocysteine to methionine by methionine synthase.

Nutritional support for Homocystinuria

Goals of nutritional support

1. To maintain plasma MET between 18 and 45 µmol/L
2. Maintain plasma CYS between 25 and 50 µmol/L
3. Maintain homocysteine in blood at <100 µmol/L
4. Support normal growth and development
5. Prevent catabolism

- **What to calculate:**
  1. MET:
     a) Prescribe MET intake that support normal growth (Table 1).
  2. CYS :
     a) Prescribe CYS intake that maintains treatment plasma CYS concentration (Table 1).
  3. Protein:
     a) Prescribe amount greater than RDA (Table 1).
  4. Energy:
     a) Prescribe amount that should support normal weight gain in infant and children and maintain appropriate weight for height in adult (Table 1).
  5. Fluid:
     a) Prescribe amount that will supply water requirement (Table 1)
     b) Offer 1.5 ml/kcal and 1.0 ml/kcal for neonates and children respectively.
- **How to calculate:** (3.0 kg new born baby)
  1. nutrients requirements :

Energy 95-145 kcal/kg	Protein 3-3.5 gm/kg	Methionine 15-30 mg/kg	Cystin 300 mg/kg
390 kcal/day	10.5 gm/day	90 mg/day	900 mg/day

2. MET
   a) Calculate amount of infant formula or table foods required to fill MET prescription

1gm Similac ➔ 2.71mg MET

90 ÷ 2.71 = 33gm Similac

   b) Measure infant formula on scale that read in grams
   c) Add table food gradually to displace MET provided by infant formula if the patient is developmentally ready
3. Protein
   a) Calculate the amount of protein from the infant formula or food table that required to fill the MET prescription

1gm Similac ➔ 0.118gm protein

33gm Similac = 3.9gm protein

   b) Subtract amount determined above from total protein prescription

10.5gm – 3.9gm= 6.6gm protein remaining

c) Supply any remaining prescribed protein with Hominex

> 1gm Hominex ➔ 0.15gm protein
>
> 6.6gm protein ➔ 44gm Hominex

d) Hominex-1 is for infant and toddlers and Hominex-2 is for children and adults (Table 3)
e) Measure Hominex powder by scale that reads in grams

4. CYS
   a) Calculate amount of CYS provided by infant formula or table foods required to fill MET prescription
   b) Calculate amount of CYS supplied by Hominex required to fill protein prescription
   c) Added together, values calculated above should fall within range of CYS requirement (Table 1)
   d) If not, supplement the remaining as pure suspension (only if plasma CYS is below normal)
5. Energy
   a) Calculate energy provided by infant formula or table foods and Hominex required to fill MET and protein prescriptions

33gm Similac = 173 kcal
44gm Hominex = 211 kcal
173 + 211 = 384 kcal/day
384 kcal ÷ 3kg = 128kcal/kg
Meet patient's needs

b) Subtract amount determined above from total energy prescription
c) Provide remaining prescribed energy with Ploycose (3.8 kcal/gm) or Prophree (5.2 kcal/gm) if needed.

6. Fluid :
   a) Add sufficient water to infant formula, synthetic protein and the energy supplement and mix in sterilized, tightly closed container by shaking for 10 to 12 seconds.
   b) Refrigerate in sterilized, closed containers until used. Discard unused formula after 24 hours.
   c) Provide parents, caregiver with completed Diet Guide.
   d) Feed young infants 6-8 times daily, feed children and adults 4-6 times daily.

Regular concentration: 20 kcal/oz.

384 kcal ➔580 cc water/day

Monitoring and Evaluation of nutrition support:

1. Plasma MET, CYS, and Homocysteine concentrations
   a) Initially evaluate twice weekly until stabilized and approximate dietary MET and CYS requirements are known.
   b) Ongoing, frequent evaluation (monthly) helps to ensure adherence to nutritional support plan.
   c) Unacceptable MET concentrations:
      - If >45µmol/L, subtract 5 to 10 % from the prescribed MET and reevaluate in 7 days
      - If continues >45 µmol/L, repeat above process until value is in treatment range.
      - If low, add 20mg to prescribe MET and reevaluate plasma concentration in 7 days.

Protein status

1. Evaluate pre-albumin every 3 months until patient is 1 year of age and every 6 months thereafter
2. If pre-albumin is below standard: increase prescribed protein by 5-10% and reevaluate in 1 month.
3. If plasma MET, CYS, and homocysteine are in treatment range, use Hominex to increase protein.

Growth status:

1. Monitor weight and height with every clinic visit and must be plot on NCHS growth charts.
2. If patient remains below usual growth channel and does not respond to increase in protein and energy or cannot consume diet prescribed through oral

feeding, nasogastric or gastrostomy tube feeding should be considered.

3. Maintain records of food intake for 3 days immediately before each blood test.

Example:

New born baby with Homocystinuria weigh 3kg:

Nutrients Requirements:	**Give:**
• Energy 95-145 kcal/k/day	390 kcal/day
• Protein 3-3.5 gm/kg/day	10.5 gm/day
• Methionine 15-30 mg/kg/day	90 mg/day
• Cystin 300mg/kg/day	900 mg/day

100% NP	**Amount (gm)**	**MET (mg)**	**CYT (mg)**	**Protein**		**Energy Kcal**
				NP gm	AA gm	
Similac	33	90	-	3.9		173
Hominex-1	44				6.6	211
Total\d				10.5		384
Total \kg				3.5		128

580 cc water/day

50 % NP	Amount (gm)	MET (mg)	CYT (mg)	Protein		Energy Kcal
				NP gm	AA gm	
Similac	17	46	-	2		89.42
Hominex-1	57				8.55	273.6
Prophree	5					26
Total\d				10.55		389
Total \kg				3.5		129

580 cc water/day

Table 1: Recommended daily nutrient intakes (ranges) for infants, children , and adults with Homocystinuria .

Age	Nutrient				
	MET[1,2] (mg/kg)	CYS[2] (mg/kg)	Protein[3,4] (g/kg)	Energy[3,4] (kcal/kg)	Fluid[5] (mL/kg)
Infants					
0 to < 3 mo	15 - 30	300	3.50 - 3.00	120 (145 - 95)	150 - 125
3 to < 6 mo	10 - 25	250	3.50 - 3.00	115 (145 - 95)	160 - 130
6 to < 9 mo	10 - 25	200	3.00 - 2.50	110 (135 - 80)	145 - 125
9 to < 12 mo	10 - 20	200	3.00 - 2.50	105 (135 - 80)	135 - 120
	(mg/kg)	(mg/kg)	(g/day)	(kcal/day)	(mL/day)
Girls and Boys					
1 to < 4 yr	10 - 20	100 - 200	≥ 30.0	1,300 (900 - 1800)	900 - 1,800
4 to < 7 yr	8 - 16	100 - 200	≥ 35.0	1,700 (1300 - 2300)	1,300 - 2,300
7 to < 11 yr	6 - 12	100 - 200	≥ 40.0	2,400 (1650 -3300)	1,650 - 3,300
Women					
11 to < 15 yr	6 - 14	50 - 150	≥ 50.0	2,200 (1500 - 3000)	1,500 - 3,000
15 to < 19 yr	6 - 12	25 - 125	≥ 55.0	2,100 (1200 - 3000)	1,200 - 3,000
≥ 19 yr	4 - 10	25 - 100	≥ 60.0	2,100 (1400 - 2500)	1,400 - 2,500
Men					
11 to < 15 yr	6 - 14	50 - 150	≥ 55.0	2,700 (2000 - 3700)	2,000 - 3,700
15 to < 19 yr	6 - 16	25 - 125	≥ 65.0	2,800 (2100 - 3900)	2,100 - 3,900
≥ 19 yr	6 - 15	25 - 100	≥ 70.0	2,900 (2000 - 3300)	2,000 - 3,300

Table 2: Serving lists for MET restricted diets: Average nutrient content per serving

Food list	Nutrient			
	MET(mg)	CYS (mg)	Protein(g)	Energy (kcal)
Breads/Cereals	20	20	1.2	55
Fats	2	0	0.1	50
Fruits	5	5	0.5	60
Vegetables	10	8	1	20

Table 3: Nutrient composition of Hominex-1 and Hominex-2

Nutrient	Hominex-1*		Hominex-2	
	(per 100 g pwd)	(per g protein equiv)	(per 100 g pwd)	(per g protein equiv)
Energy, kcal	480	32	410	13.7
Protein equiv, g	15.00	1.000	30.00	1.000
Nitrogen, g	2.40	0.160	4.80	0.160
Amino acids, g	17.67	1.178	35.34	1.178
Cystine, g	0.45	0.030	0.90	0.030
Histidine, g	0.42	0.028	0.84	0.028
Isoleucine, g	1.08	0.072	2.16	0.072
Leucine, g	1.68	0.112	3.36	0.112
Lysine, g	1.00	0.067	2.00	0.067
Methionine, g	Trace	0	Trace	0
Phenylalanine, g	0.88	0.059	1.76	0.059
Threonine, g	0.70	0.047	1.40	0.047
Tryptophan, g	0.17	0.011	0.34	0.011
Tyrosine, g	0.89	0.059	1.78	0.059
Valine, g	1.22	0.081	2.44	0.081
Other Nitrogen-Containing Compounds				
Carnitine, mg	20	1.33	40	1.33
Taurine, mg	40	2.67	50	1.67
Carbohydrate, g	53.0	3.53	35	1.17
Fat, g	21.7	1.45	14	0.47
Linoleic acid, g	2.00[4]	0.133	1.50[5]	0.050
α-Linoleic acid, g	0.36[6]	0.024	0.17[7]	0.006
Minerals				

Calcium, mg	575	38	880	29
Chloride, mg/mEq	435/12.27	29.0/0.82	1,160/32.72	38.7/1.09
Chromium, µg	11	0.73	27	0.90
Copper, mg	1.10	0.073	1.00	0.033
Iodine, µg	65	4.33	100	3.33
Iron, mg	9.0	0.60	13	0.43
Magnesium, mg	50	3.33	225	7.50
Manganese, mg	0.50	0.033	0.80	0.027
Molybdenum, µg	12	0.80	30	1.00
Phosphorus, mg	400	27	760	25
Potassium, mg/mEq	675/17.26	45/1.15	1,370/35.04	45.7/1.17
Selenium, µg	20	1.33	35	1.17
Sodium, mg/mEq	190/8.26	12.70/0.55	880/38.28	29.3/1.28
Zinc, mg	8.0	0.53	13	0.43
Vitamins				
A, µg RE	420	28	660	22
D, µg	7.50	0.50	7.50	0.25
E, mg α-TE	10.10	0.67	12.10	0.40
K, µg	50	3.33	60	2.00
Ascorbic acid, mg	50	3.33	60	2.00
Biotin, µg	65	4.33	100	3.33
B_6, mg	0.75	0.050	1.30	0.043
B_{12}, µg	4.90	0.327	5.00	0.167
Choline, mg	80	5.33	100	3.33
Folate, µg	230	15	450	15
Inositol, mg	40	2.67	70	2.33
Niacin equiv, mg	12.80	0.850	21.7	0.72
Pantothenic acid, mg	6.90	0.460	8.00	0.267
Riboflavin, mg	0.90	0.060	1.80	0.060
Thiamin, mg	1.90	0.127	3.25	0.108

Chapter 7

Standard Recipes

Standard recipe for newborn wt. 2.5kg UCD

- **100% Natural protein**

Similac	36gm
Cyclinex-1	17gm
Prophree	10gm
Water	350CC
TV	400CC

- **50% Natural protein**

Similac	18gm
Cyclinex-1	45gm
Water	350CC
TV	400CC

- **0% Natural protein**

Cyclinex-1	70gm
Water	400CC
TV	450CC

Standard recipe for newborn wt. 3kg UCD

- **100% Natural protein**

Similac	45gm
Cyclinex-1	20gm
Prophree	10gm
Water	450CC
TV	500CC

- **50% Natural protein**

Similac	23gm
Cyclinex-1	52gm
Water	450CC
TV	480CC

- **0% Natural protein**

Cyclinex-1	88gm
Water	470CC
TV	550CC

Standard recipe for newborn wt. 2.5kg MMA/PA

- **100% Natural protein**

Similac	45gm
MMA/PA anamex infant	26gm

Water	450CC
TV	500CC

- **50% Natural protein**

Similac	23gm
MMA/PA anamex infant	46gm
Water	400CC
TV	470CC

- **0% Natural protein**

MMA/PA anamex infant	65gm
Prophree	5gm
Water	400CC
TV	460CC

Standard recipe for newborn wt. 3kg MMA/PA

- **100% Natural protein**

Similac	55gm
MMA/PA Anamex Infant	30gm
Water	470CC
TV	530CC

- **50% Natural protein**

Similac	27gm

MMA/PA Anamex Infant	55gm
Water	530CC
TV	600CC

- **0% Natural protein**

MMA/PA Anamex Infant	80gm
Prophree	5gm
Water	530CC
TV	600CC

Standard recipe for newborn wt. 2.5kg MSUD

- **100 % natural protein:**

Similac	24gm
Msudanamex infant	45gm
Water	350cc
TV	400CC

- **50% natural protein:**

Similac	12gm
Msudanamex infant	55gm
Water	350cc
TV	400cc

- **0% natural protein:**

Msudanamex infant	65gm
Polycose	10gm
Water	350cc
TV	400cc

Standard recipe for new born wt. 3kg MSUD

- **100 % natural protein:**

Similac	30gm
Msudanamex infant	55gm
Water	450cc
TV	500CC

- **50% natural protein:**

Similac	15gm
Msudanamex infant	66gm
Water	420cc
TV	480cc

- **0% natural protein:**

Msudanamex infant	80gm
Polycose	10gm
Water	450cc
TV	500cc

Standard recipe for newborn wt. 2.5 kg VLCAD

Monogen	65gm
Water	325cc
Total volume	400cc
MCT oil	3cc

Standard recipe for newborn wt. 3 kg VLCAD

Monogen	78gm
Water	390cc
Total volume	480cc
MCT oil	4cc

Standard recipe for newborn wt. 2.5 kg PKU

- **100% Natural protein**

Similac	38gm
Phenex-1	30gm
Water	400CC
TV	430CC

- **50% Natural protein**

Similac	20gm
Phenex-1	43gm
Water	350CC

TV	400CC

- **0% Natural protein**

Phenex-1	60gm
prophree	10gm
Water	350CC
TV	400CC

Standard recipe for newborn wt. 3kg PKU

- **100% Natural protein**

Similac	45gm
Phenex-1	35gm
Water	450CC
TV	500CC

- **50% Natural protein**

Similac	23gm
Phenex-1	52gm
Water	400CC
TV	460CC

- **0% Natural protein**

Phenex-1	70gm
prophree	10gm
Water	450CC

TV	500CC

Standard recipe for newborn wt. 2.5kg Homocystinuria

- **100% Natural protein**

Similac	28gm
Homonex-1	35gm
Water	400CC
TV	450 CC

- **50% Natural protein**

Similac	15gm
Homonex-1	50gm
Water	400CC
TV	450CC

- **0% Natural protein**

Homonex-1	60gm
Prophree	10gm
Water	400CC
TV	470CC

Standard recipe for newborn wt. 3kg Homocystinuria

- **100% Natural protein**

Similac	33gm

Homonex-1	44gm
Water	450CC
TV	500CC

- **50% Natural protein**

Similac	16gm
Homonex-1	60gm
Water	420CC
TV	470CC

- **0% Natural protein**

Homonex-1	70gm
Prophree	10gm
Water	450CC
TV	500CC

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