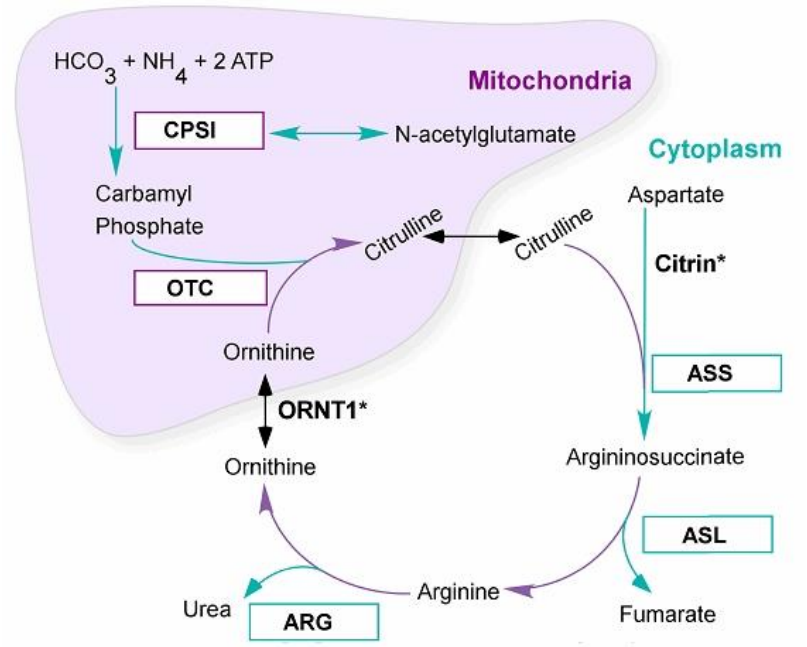
LONG TERM MANAGEMENT UREA CYCLE DISORDERS

Definition:

- Urea cycle disorders are characterized by the triad of hyperammonemia, encephalopathy and respiratory alkalosis(1-3).
- It results from defects in the metabolism of waste nitrogen from the breakdown of protein and other nitrogen-containing molecules(1, 2).
- It caused by deficiency of one of the following enzymes:
  - Ornithine transcarbamylase (OTC)
  - Carbamyl phosphate synthetase(CPS)
  - N- acetylglutamate synthetase (NAGS)
  - Argininosuccinic acid synthetase(ASS)
  - Argininosuccinic acid lyase(ASL)
  - Arginase.

Pathway:



Clinical Presentation:

- The most common defect is OTC deficiency followed by ASS deficiency
- There is considerable clinical and biochemical heterogeneity.

A. Classical neonatal form:

- Most babies of normal birth weight and are initially healthy but after short interva , they become unwell, common early symptoms are poor feeding , vomiting , lethargy ,irritability that progress to seizure ,deep coma, hyperventilation, respiratory alkalosis and even death if not treated. The liver may be enlarged and serum level of transaminase are often elevated.
- In OTC deficiency the classical form are more common in male, however, small number of female may have also similar presentation.(1-4)

B. Late onset form:

- There have been a variety of different clinical pictures in patient with partial residual activity of defective enzyme.
- All of these variant are encountered less frequently than the classic infantile one.
- Some have had a more gradual onset of difficulty of feeding and recurrent or cyclic vomiting in infancy or child hood.
- Some have had hepatomegaly and elevation of transaminase which may cause confusion by suggesting diagnosis of hepatocellular diseas.

- Episodic hyperammonemia may occure with vomiting lethargy headache ,tremor,seizures or ataxia .
- Some degree of retardation of mental development may present
- Some has bizzar behaviour and psychiatric sign.
- An encephalopathic (slow wave) EEG pattern may be observed during hyperammonemia.
- Non specific brain atrophy may be seen on MRI
- Some are asymptomatic and diagnosed because their relative have classical form.(1-4)

C. Additional clinical abnormalities:

- Dysmorphic feature include : microcephaly and dry brittle hair are seen in patient with ASS deficiency.
- Also brittle hair and hepatomegaly can be seen in patient with ASL deficiency.
- Arginase deficiency (Argininemia) its clinical picture quite different from the other disorder of urea cycle , the patient usually present with spastic diplegia diagnosed not infrequently as cerebral palsy. However, this picture might be complicated by the presence of extrapyramidal features. The head circumference drops away from the centiles and those affected become microcephalic.,ammonia may be normal or mildly elevated
- Psychomotorretardation , seizure is also common.
- Heterozygote female for OTC may present with postpartum hyperammonemia.(1-4)

Diagnosis (5):

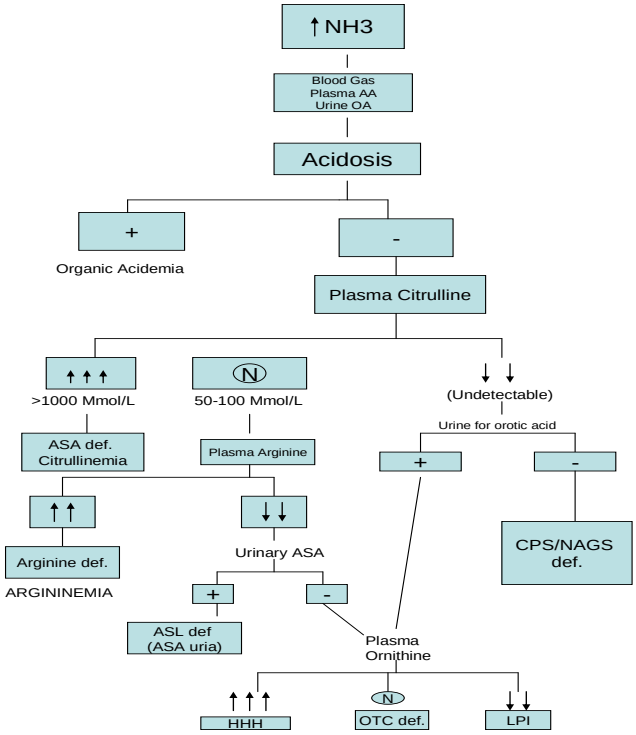


Table 1: The Most Important Diagnostic Findings in Defect of the Urea Cycle(3)

Disorder	Alternative names	Plasma aminoacids	Urine orotic acid	Tissue for enzyme diagnosis	Gene	Estimated birth prevalence
N- acetylglutamate synthetase deficiency	NAGS deficiency	Increase glutamine and alanine	Normal	Liver	NAGS	Very rare
Carbamyl phosphate synthetase deficiency	CPS deficiency	Increase glutamine and alanine Decrease citrulline and arginine	Normal	Liver	CPS1	1:56000
Ornithine transcarbamylase deficiency	OTC deficiency	Increase glutamine and alanine Decrease citrulline and arginine	Increase	Liver	OTC	1:15000
Argininosuccinate synthetase deficiency	ASS deficiency, citrullinaemia type 1	Increase glutamine , alanine and citrulline Decrease arginine	Increase	Liver or fibroblast	ASS1	1:60000
Argininosuccinate lyase deficiency	ASL deficiency Argininosuccinic aciduria (ASA)	Increase glutamine , alanine , Citrulline, and argininosuccinate Decrease arginine	Increase	Liver or fibroblast or RBC	ASA	1:70000
Arginase deficiency	hyperargininaemia	Increase arginine	Increase	Liver or RBC	ARG1	

Treatment:

1. **Acute episode treatment guidelines (Emergency):**
   - ABC (or now CAB).
   - Stop all source of protein central and parenteral nutrition.
   - Call the pharmacy to prepare the medications and lipid (see dosages below)
   - Check GlucoChecks.
   - Insert an IV line (central and peripheral) and take blood for blood gases, chem 1, liver enzymes, ammonia (NH3), & CBC, blood C/S (peripheral and central if patient has central line). As **STAT** order. Other labs as needed.
   - Start 1 1/2 to double maintenance I.V.F as D10 1/2NS. Re-adjust according to lab results (Keep GlucoChecks 5-8mmol/L). Consider start insulin if hyperglycemia develop at dose of 0.01-0.05 unit/kg/hour and titrate up until blood glucose controlled. Total glucose requirements: 6-8mg/kg/minutes.
   - The amount of potassium supplement through IV line according to the potassium level result :
     - >5.5 = No kcl will be added
     - 3.5-5.5= kcl 20 meq/l .If he is on Ammonul : kcl 30 meq/l
     - <3.5= 40 meq/l
     - <2.8 = 0.5 meq/kg kcl as a bolus in prediluted solution D5 w over one hour (should be given centrally and patient should be attached to cardiopulmonary monitor during the

infusion) or you can give the required dose of kcl through PO/GT if he can tolerate it. KCL can be given through peripheral line up to 60 meq/l, rate must not exceed 0.125meq/kg/hour.

- If ammonia >100 umol/l. Start intralipid 20% at 2-3 g/kg/day to provide additional calories.
- Give a loading dose of ammonia scavengers medications as intravenous infusion over 90 minutes followed by the same maintenance dose divided over 24 hours (see table 2).

Table2: Recommended dosages for medications used in acute management of urea cycle disorders (6,7):

	Arginine HCl		Ammonul® (see appendix 3)		N-carbamylglutamate (Carbaglu®)
Kg	<20kg	>20kg	<20	>20	Only oral/enteral drug)
Pending diagnosis	250-400mg/kg(6). Up to 600mg/kg was recommended(7)	250-400 mg/kg(6) Up to 600mg/kg was recommended(7)	250mg/kg	5.5gram/m^2	100mg/kg bolus per NG tube then 25–62.5mg/kg every 6h(6)
NAGS deficiency	250mg/kg(6)	250mg/kg(6)	Not indicated		Same as above (6)
CPS or OTC deficiency	250mg/kg(6)	250mg/kg(6) or 4000mg/m^2/day(2)	250mg/kg Maintenance dose up to 500mg/kg/day(6)	5.5gram/m^2	Not indicated
ASL deficiency	200-400mg/kg(6) Up to 600mg/kg was recommended(7)	200-400mg/kg(6) or 12000mg/m^2/day(2)	Same as above		Not indicated
Arginase deficiency	Not indicated		Same as above		Not indicated

Note:

- Arginine HCl, lipid and KCl could be given at peripheral line at the same line (unpublished data from experts)
- Repeat ammonia, blood gases, chem 1 after the loading dose completed.
- Reloading has to be done carefully, in particular during the first 24 h, as cumulative doses of >750 mg/kg/24 h of AMMONUL® have been shown to be associated with development of toxicity (vomiting, lethargy). Reloading only in neonates with severe disorders or those who are undergoing dialysis, and should be spaced at least 6 hours.
- Ensure enough caloric intake covering 110% of the recommended daily allowance (RDA) in order to shut down endogenous protein breakage (RDA: for newborn and infant: 110-120 kcal/kg/day, for 1-3 yrs:100, for 4-6yrs: 90, for 7-10yrs: 70, for 11-14yrs: 50-55).
- Do not decrease dextrose rate or amount and DO NOT STOP calorie delivery in the acute stage for any reason (e.g. medications, addition required fluid bolus, or hyperglycemia) as this can precipitate hypoglycemia and catabolism which will further worsen the patient's condition.
- According to clinical evaluation, empirical antibiotics may be started.
- Ammonia, electrolyte and blood gases need to be followed at regular intervals during this acceleration of management stage. The frequency is dictated by the patient's condition and the speed at which results can be obtained.
- DO NOT STOP other oral chronic medications.

- Give prophree or polycose through PO/NG as tolerated
- Call metabolic dietitian on call
- If ammonia <100 start Cyclinex formula with 50% natural protein.
- Proteins should be re-introducing within 24 hours-36 hours of initiation of therapy even if the patients on dialysis.
- Start dialysis if above measures failed to reduce ammonia within4 hours or if initial ammonia is >500 μmol/L.(2, 6-9) see appendix1.

Table 3: Other acute treatment issues (2, 6-9):

• **pressors, buffering agent**	• Depending on the cardiovascular and acid-balance status of the infant is also important.
• **Oncotic agent such as albumin**	• In selected cases and on limited bases can be used because will contribute to overall nitrogen load.
• **Intubation**	• It is preferable to perform it on infants with borderline clinical condition before transport or before they have respiratory compromise • For 2 reasons: (1) if a patient is breathing rapidly respiratory alkalosis driven by cerebral edema), excess calories are burned, contributing to catabolism and further nitrogen accumulation, (2) Intubation is a difficult procedure to carry out while an infant is being transported and can lead to hypoxia.
• **Antibiotics**	• With heavy instrumentation and stress preferred to continue or initiate them as prophylaxis.
• **Hyperventilation**	• Recommended
• **Mannitol**	• Has not been demonstrated to be effective in managing cerebral edema caused by hyperammonemia
• **Steroid**	• Should be avoided • Because they will increase the amount of protein turnover and hence increase the nitrogen load.
• **Glucose and insulin**	• can serve as suppressors of catabolism, but their use requires care. • Administer 6 to 8 mg/kg/min of glucose (administered as 10% dextrose in water) and to use insulin sparingly to maintain the serum glucose level <170 mg/dl (9.5 mmol/l). • The presence of glycosuria is an indication for continued administration of intravenous regular insulin at a rate that keeps glucose levels between 120 and 170 mg/dL(6.6 -9.5 mmol/l)
• **Carnitine**	• Not believed to be beneficial. Except if there is documented carnitine deficiency during monitoring
• **Valproic acid**	• Should be avoided in any patient who has seizure. • It is known to decrease urea cycle function and will aggravate the hyperammonemia
• **NaHCO3**	• Not recommended, Patient with urea cycle usually has respiratoly alkalosis. Hyperchloremic acidosis may result from arginine hydrochloride or dehydration which can be treated either by holding arginine or giving IV fluid.
• **Citrulline**	• Used in neonates with UCD and CPS or OTC deficiencies. • The rationale being that pulling aspartate into the pathway may increase nitrogen clearance. • The dose of citrulline used is 150 to 200 mg/kg/24 h. • A clear diagnosis should be made before citrulline is used to avoid providing citrulline to patients with ASS and ASL who already have excessive amounts of this amino acid.

3. Long term management (home and outpatient visits)

a. Nutritional management:

The aim of dietary management includes:

- Normal weight gain, linear growth, and head growth.
- Normal psychomotor development, as assessed by serial examinations and valid developmental screening tools (e.g., Denver Developmental Screening Test II).
- Protein is restricted in the diet to provide limited amounts of isoleucine, methionine, threonine, valine and odd chain fatty acids and the further supplemented with aminoacids mixture to provide additional amino acids without the offending amino acids (see table 1 and 2).
- Avoidance of essential amino acid, fatty acid, and micronutrient deficiencies.

Metabolic dietitian should ensure the following:

- Home formula supplies include aminoacids mixture eg: CYCLINEX®-1 (for infant and toddler), CYCLINEX®-2 (for children; adolescents, and adults) see appendix 3.
- For infant: Breast milk or regular formula as a natural protein source. For older children: the source of natural protein from regular diet.
- Compliance of the mother with weighing skills, appropriate preparation of formula and 3-days diet records prior to clinic visit.
- Monitoring of amino acid concentrations. The frequency of amino acid monitoring varies by age, metabolic stability, compliance, and regional clinical practice. For rapidly growing infants, monitoring weekly is recommended (see monitoring section).

Table 4: Treatment Ranges for Target Amino Acids in urea cycle disorders:

Amino Acid (µmol/l)	(2-4 hr 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
ILEUCINE	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

Note: These levels based on BC Children Hospital reference ranges. The optimal level depends on the normal range for age established in the local laboratory.

Biochemical target for optimal urea cycle control(10):

- Plasma ammonia <40 µmol/L.
- Plasma glutamine <1000 µmol/L.
- Normal plasma levels of alanine, glycine, lysine, and arginine
- No subnormal concentrations of essential amino acids (eg, leucine, isoleucine, valine).
- Normal urinary orotate excretion (<3 µmol/mmol creatinine).
- Normal plasma protein concentrations (eg, albumin).

Table 5: Recommended daily nutrient intake in urea cycle disorders (11)

Age	Total Protein (g/kg)	Energy (kcal/kg)	Fluid (mL/kg)
Infants			
0 to <3 mo	2.20–1.25	150–125	160–130
3 to <6 mo	2.00–1.15	140–120	160–130
9 to <12 m	1.60–0.90	120–110	130–120
Girls and boys	(g/day)	(kcal/day)	(mL/day)
1 to <4 yr	8–12	945–1890	945–1890
4 to <7 yr	12–15	1365–2415	1365–2445
7 to <11 yr	14–17	1730–3465	1730–3465
Women	(g/day)	(kcal/day)	(mL/day)
11 to <15 yr	20–23	1575–3150	1575–3150
15 to <19 yr	20–23	1260–3150	1260–3150
≥19 yr	22–25	1785–2625	1875–2625
Men	(g/day)	(kcal/day)	(mL/day)
11 to <15 yr	20–23	2100–3885	2100–3885
15 to <19 yr	21–24	2200–4095	2200–4095
≥19 yr	23–32	2625–3465	2625–3465

Table 6: safe daily protein intake in urea cycle disorders (6)

Age	1 m	2m	3m	6m	12m	18m	2y	3y	4-6	7-10	11-12
Protein intake (gm/kg/day)	1.77	1.50	1.36	1.31	1.14	1.03	0.97	0.90	0.87	0.92	0.90

Disorder	Sodium benzoate	Sodium phenylbutyrate	L-Arginine (hydrochloride or free base)	L-Citrulline	Carbamylglutamate (carbaglu®)
NAGS deficiency	Not indicated	Not indicated	Not indicated	Not indicated	10–100 mg/kg/day
CPS1deficiency	≤ 250mg/kg/day maximum: 12g/day	<20 kg: ≤250mg/kg/day >20 kg: 5g/m^2/day maximum: 12g/day	<20kg:100-200mg/kg/day >20kg: 2.5-6g/m^2/day Maximum: 6g/day	100-200mg/kg/day Maximum: 6g/day	Not indicated
OTC deficiency	Same	Same	Same	Same	Not indicated
ASS and ASL deficiency	Same	Same	<20kg:100-300mg/kg/day >20kg: 2.5-6g/m^2/day Maximum: 8g/day	Not indicated	Not indicated
Arginase deficiency	Same	Same	Not indicated	Not indicated	Not indicated

- Protein requirements for child with urea cycle disorders varies depend on the age and growth rate and severity of the disease.
- For patient with severe disease some of natural protein (a mixture of essential and non essential aminoacid may be replaced with an essential aminoacid mixture (20-30%)(6)
- Requirement for many trace element and vitamins in children with urea cycle disorders have not been established.
- Several of the supplements appear to be very low in vitamin B12 in the their diet , some centers measure urinary methylmalonic acid to monitor the adequacy of their supplement.

Table 7: Chronic medications for life (6):

Note:

- Sodium PBA was considered of second choice for long-term treatment by most guideline group members. It should be given together with sodium benzoate in patients in which benzoate alone is not enough.(6)
- Serum/plasma levels of benzoate/PBA and plasma levels of arginine (aim are fasting levels of 70–120 µmol/L) should be monitored to adjust dosages and in case of high or repeated doses.(6)
- L-Arginine: higher doses are needed in some patients according to expert advice. are 400-700mg/kg/day in children of <20kg, and, >20 kg: 8.8-15.4 g/m2/day.(10)
- Sodium phenylbutyrate: higher doses are needed in some patients according to expert advice: <20: 450-600mg/kg/day. >20kg: 9-13 g/m2/day.(10)
- Citrulline may be preferable. When given no need for concomitant use of L-arginine.(6)

Monitoring (6, 11)

A. Clinical monitoring:

- ✓ Weight, height, and head circumference
- ✓ Developmental assessment
- ✓ Neurologic assessment
- ✓ Liver examination

B. Biochemical lab monitoring :

- ➢ Plasma amino acid and ammonia weekly since diagnosis till 6months of age then every other week till 1year then monthly .
- ➢ Ammonia target less than 40micromol/l (in other reference: <80micromol/l)(6).
- ➢ Plasma glutamine target less than 1000 micromol/ l, however, high glutamine concentration do not invariably indicate encephalopathy.
- ➢ Normal concentration of essential amino acid (eg : leucine ,isolucine,valine)
- ➢ Normal urinary orotate excretion less than 3 micromol/l creatinine.
- ➢ CBC ,Retic, Ca ,Phosphorus , AST,ALT ,GGT, alkaline phosphatase, vitamine B12, zinc, selenium, urine for orotic acid, lipid profile, blood sodium benzoate and/or sodium PBA/phenylacetate assays to be done every 3 month until 1year age then every 6 months.
- ➢ Albumin and prealbumin monthly until 1 year then every 3 months.
- ➢ Plasma ferritin concentration evaluate at 6,9, 12 months then every 6 months.
- ➢ Magnetic resonance imaging (MRI) early on in each coma or stroke-like episode, and at 2-year intervals.

C. Other monitoring parameters :

Age(years)	0.5	1	2	3	4	5	6	9	12	15
EEG	*	*		*		*				
Bone Age	*		*		*		*	*	*	*
Bone densitometry		*		*		*		*		

D. Clinic follow up :

- **Metabolic and Dietitian clinic :** every 2 months till 1 year of age then every 3 months till 6 years of age then every 6 months till 17 years of age then every year
- **Neurology clinic:** at Dx then every 6 months till 1 year then every 2 years till 9 years of age then at 15 years of age .
- **Psychology clinic:** at 3 years of age then every 2 years till 9 years then at 13 and 15 years**.**
- **Physiotherapy :** at Dx then at 4 months ,8months, 18 months ,3 years,5 years**.**
- **Occupational therapy :** at 18 months , 3 years.
- **Social service:** at Dx then at 1 year and 3 years.

Note: this is general guidelines for monitoring that could be adjusted on individual basis.

Sick day management:(10)

- In females with deterioration during or prior menstruation, instituting a "sick day" dietary regimen for the premenstrual or menstrual period would seem reasonable**.**
- Home Sick-day regimen is also indicated in case of URTI, trauma, surgery etc**.**
- Reduce protein intake to 50% for 24 to 48 h
- Increase total calories by 10 to 25%
- 1 -1.5 imes increased fluid intake
- Maximize Na phenylbutyrate if possible**.**
- Maximize arginine hydrochloride if possible**.**
- Aggressively treat the underlying illness**.**
- If the patient does not improve within 24-48 h – bring the patient to ER

Management with immunizations:**(10)**

- Give sick day formula 50% for 24 hours
- manage fever >38 C with ibuprofen. Acetaminophen should be avoided because this drug could be hepatoxic, especially in large doses.
- If not improved within 24 hours bring to ER

Management with surgical procedure:**(10)**

- Ensure that the patient on his usual state of health prior to procedure
- Ensure stability of metabolic parameters including leucine, isoleucine and valine prior to procedure**.**
- Plasma aminoacids, chem1, blood gas, prior to procedure.
- High caloric intake with IVF D10 and lipid which provide 110 to 120% of normal energy needs starting 12-24 hours prior to procedure.
- After surgery follow the guidelines mentioned in Transition to long term management (Wards protocol).

Liver transplantation:

- Liver transplantation should ideally be carried out before irreversible neurological damage and/or repeated crises, generally between 3 and 12 months of age and/or 5 kg body weight.(6)
- For those suffering recurrent metabolic decompensation and hospitalizations despite medical therapy, as well as those with poor quality of life.(12)
- Standard orthotopic liver transplantation (OLT) is preferred to auxiliary liver transplantation because it has fewer complications.(13)
- Transplantation of liver lobes from living relatives can reduce waiting times and gives results comparable to those obtained with cadaveric organs, albeit that it entails a small risk for donors. Heterozygosity for the disease in the living related donor is not a problem, except in OTCD females, although asymptomatic OTC heterozygotes have been successful donors.(14)

Appendix 1:

- Hemodialysis is the preferred method.
- Continuous arteriovenous hemodialysis (CAVHD) or continuous venovenous hemodialysis (CVVHD) with flow rates greater than 40 to 60 mL/min is optimal. Some centers use extracorporeal membrane oxygenation (ECMO) with hemodialysis. Although this combination of techniques provides very high flow rates (170-200 mL/min) and rapidly decreases ammonia levels, morbidity is greater because of the need for surgical vascular access.
- Nitrogen scavenging therapy needs to be continued during hemodialysis.
- Continue nitrogen scavenging therapy for 12-24 hours after the patient has been stabilized and is able to accept enteral feeds and medications.(15)

Appendix 2(15)

Table 8: normal ammonia level by age

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

Note: The optimal level depends on the normal range for age established in the local laboratory.

Appendix3:

AMMONUL® (information from Ucyclyd Pharma, Inc)

- AMMONUL® contains 30.5 mg of sodium per mL of undiluted product. Thus, AMMONUL® should be used with great care, if at all, in patients with congestive heart failure or severe renal insufficiency, and in clinical states in which there is sodium retention with edema. If an adverse reaction does occur, discontinue administration of AMMONUL®, evaluate the patient, and institute appropriate therapeutic countermeasures.
- Administration must be through a central line. Administration through a peripheral line may cause burns. However, experience from King Faisal Specialist Hospital that could be given through peripheral line.
- Can be given at the same line with potassium.

Appendix4:

Table 9: Differences between 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	15.00	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-Linolenic 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	7.3
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

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