Fact Sheets

Information for **DOCTORS** about the disorders included in the Expanded Newborn Screening Panel

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3– METHYLCROTNYL CoA CARBOXYLASE DEFICIENCY [3-MCC]

What is 3-MCC?

3-MCC is usually a benign autosomal recessive disorder caused by the deficiency or absence of 3-methylcrotonyl CoA carboxylase enzyme that is important in the breakdown of leucine. Children born with this condition may remain asymptomatic or may present with seizures, drowsiness, low muscle tone, failure to thrive and poor appetite.

Long term management

Long term treatment of symptomatic infants based on mildly protein restricted diet results in general improvement and reduction in the number of exacerbations. Glycine supplementation at 175 mg/kg/day increases the excretion of 3 methylcrotonylglycine. Carnitine supplementation at 100 mg/kg/day corrects the very low plasma carnitine levels and increases the excretion of 3 hydroxyisovaleric acid. It has been found that neonates who test positive for this condition in expanded newborn screening do not actually have the condition but instead reflect the increased levels of the metabolites of their mothers.

BETA-KETOTHIOLASE DEFICIENCY

What is Beta-Ketothiolase Deficiency?

Beta-Ketothiolase Deficeincy is an autosomal recessive disorder caused by the deficiency or absence of the mitochondrial acetoacetyl-CoA enzyme which breaks down the amino acid isoleucine. This in turn will lead to build up of toxic organic acids in the body. Children born with this condition appear normal at birth but untreated patients may present with low blood sugar which can lead to seizures, metabolic acidosis, coma and death.

Treatment of Beta-Ketothiolase Deficiency

Treatment is through the dietary restriction of protein. Carnitine supplementation is also given.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state, correct the acidosis and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Monitor glucose levels. May request for investigations i.e. CBC, blood gas, urine ketones as needed. May give fluid boluses if patient requires.
d. Start D10% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Monitor input and output strictly (q6 hours).

If unwell and is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with a high glucose formula
b. Insert IV access. Monitor glucose levels. May request for investigations i.e. CBC, blood gas, urine ketones as needed. May give fluid boluses if patient requires.
c. Start D10% 0.3 NaCl at 5-10 cc/hr.
d. Monitor input and output strictly (q6 hours).

* Inform metabolic doctor on call for further guidance regarding on-going management.

BIOTINIDASE DEFICIENCY

What is Biotinidase Deficiency?

Biotinidase deficiency is an autosomal recessive disorder caused by the deficiency or absence of the enzyme biotinidase. This enzyme is needed to produce biotin which in turn is needed by the carboxylase enzymes to work properly. Untreated children born with this condition may present with lethargy, seizures, hyptotonia, vomiting and a skin rash. Patients may also present with hyperammonemia and severe metabolic acidosis.

Treatment of Biotinidase Deficiency

Treatment is through biotin supplementation at 5-10 mg/day. The clinical response to treatment is dramatic, ketosis and acidosis disappear along with hyperammonemia, lethargy, hypotonia and ataxia. The dermatological effects of the disorder are likewise reversed.

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CARNITINE PALMITOYL TRANSFERASE TYPE 1 DEFICIENCY [CPT1 deficiency]

What is CPTI Deficiency?

Carnitine Palmitoyl Transferase Type I (CPT1) Deficiency is an autosomal recessive disorder caused by the deficiency or absence of the Carnitine Palmitoyl Transferase Type I enzyme needed for beta-oxidation. Children born with this condition appear normal at birth but untreated patients may present with low blood sugar and liver disease which can lead to seizures, coma and death.

Treatment of CPT1 Deficiency

Treatment is through the dietary restriction of fat. Patients may benefit from a special milk formula containing medium chain triglycerides.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent hypoglycemia.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Monitor glucose levels. Collect samples for urine ketones. May request for other investigations (i.e. CBC, CK, liver transaminases, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D10% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Monitor input and output strictly (q6 hours).

If unwell and is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with a high glucose formula
b. Insert IV access. Monitor glucose levels. Collect samples for urine ketones. May request for other investigations (i.e. CBC, creatine kinase, liver transaminases, blood gas) as needed. May give fluid boluses if patient requires.
c. Start D10% 0.3 NaCl at 5-10 cc/hr.
d. Monitor input and output strictly (q6 hours).

* Inform metabolic doctor on call for further guidance regarding on-going management.

CARNITINE PALMITOYL TRANSFERASE TYPE II DEFICIENCY [CPT2 deficiency]

What is Carnitine Palmitoyl Transferase Type II Deficiency?

Carnitine Palmitoyl Transferase Type II (CPT2) Deficiency is an autosomal recessive disorder caused by the deficiency or absence of the Carnitine Palmitoyl Transferase Type II enzyme needed for beta-oxidation. Children born with this condition appear normal at birth but untreated patients may present with low blood sugar which can lead to seizures, coma and death.

Treatment of CPT2 Deficiency

Treatment is through the dietary restriction of fat. Patients may benefit from a special milk formula containing medium chain triglycerides. Carnitine supplementation is also given.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent hypoglycemia.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Monitor glucose levels. Collect samples for urine ketones and serum creatine kinase (CK). May request for other investigations (i.e. CBC, liver transaminases, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D10% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Monitor input and output strictly (q6 hours). Check color of the urine and may request for urinalysis to check for urine myoglobin.

If unwell and is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with a high glucose formula
b. Insert IV access. Monitor glucose levels. Collect samples for serum CK. May request for other investigations (i.e. CBC, liver transaminases, blood gas) as needed. May give fluid boluses if patient requires.
c. Start D10% 0.3 NaCl at 5-10 cc/hr.
d. Monitor input and output strictly (q6 hours). Check color of the urine and may request for urinalysis to check for urine myoglobin.

* Inform metabolic doctor on call for further guidance regarding on-going management.

CONGENITAL ADRENAL HYPERPLASIA

What is Congenital Adrenal Hyperplasia (CAH)?

Congenital Adrenal Hyperplasia (CAH) is a group of disorders resulting from enzymatic defects in the biosynthesis of steroids. There are many enzymes involved in the synthesis of adrenal hormones but in about 90% of CAH, it is due to 21-dydroxylase deficiency. Others are due to cholesterol desmolase 11β-hydroxylase deficiency, 17β-hydroxylase deficiency and 3β-hydroxysteroid dehydrogenase. All forms of CAH are inherited in an autosomal recessive pattern. The Philippine NBS data as of December 2013 reports that 1 out of 13 350 screened newborns have CAH.

Pathophysiology

21-Hydroxylase deficiency results in decreased cortisol and aldosterone production which in turn causes increased adrenocorticotropic hormone (ACTH) secretion. High ACTH levels result in hyperplasia of the adrenal cortex. The precursor steroids behind the block are diverted to the androgen biosynthetic pathway, resulting in excess production of androgens that cause virilization in females and precocious puberty in males. The decrease in the production of aldosterone in CAH results in salt and water imbalance.

Clinical Features

- Salt-wasting
- Simple virilizing
- Late onset

Neonates with the salt-wasting (SW) form manifest adrenal crisis in the first 2-4 weeks of life characterized as poor feeding, vomiting, loose stools or diarrhea, weak cry, failure to thrive, dehydration and lethargy. If untreated, the affected newborn will die in a severe salt-losing crisis with hypoglycemia and hypotension. The baby who survives may have brain damage. Affected females usually present with ambiguous genitalia.

Diagnosis

Newborn Screening for 21-hydroxylase deficiency is done by measuring the 17-OHP level on dried blood spot. Infants with normal birth weight and a mild elevation of 17-OHP undergo repeat dried blood spot collection. Infants with moderate to severe elevation of 17-OHP and those who are low birth weight with mild elevation are referred to a pediatric endocrinologist for evaluation. Plasma 17-OHP, Na, K, cortisol and RBS are requested to confirm the condition. In cases of discrepancies between the plasma 17-OHP and clinical parameters, more extensive diagnostic evaluation is recommended: ACTH stimulation test and/or DNA mutation studies.

Treatment and Monitoring

The mainstay of treatment in CAH is glucocorticoid and mineralocorticoid replacement therapy which corrects the cortisol deficiency and reverses the abnormal hormonal patterns. Patients with deficiencies of mineralocorticoids require the appropriate replacement hormones. Glucocorticoid replacement must be increased during periods of stress. The majority of female patients with prenatal virilization require surgical repair. Heterozygous carrier detection, prenatal diagnosis, and prenatal therapy are available for families with 21-hydroxylase deficiency and are often used in 11β-hydroxylase deficiency. Regular endocrine clinic visits for monitoring of physical growth and development as well as biochemical 17-OHP and/or cortisol measurements are recommended for optimal management. Genetic counseling is recommended.

PROGNOSIS

Newborn screening makes early diagnosis and early treatment possible. Early treatment to prevent adrenal crisis is lifesaving in cases of salt-wasting CAH. Early diagnosis prevents inappropriate sex assignment for affected females of the simple virilizing (SV) form. This is very important due to the psychological and legal implications of wrong gender assignment. Progressive effects of excess androgens such as short stature and psychosexual disturbance in male and female patients are also prevented if appropriate treatment is given and monitored closely.

CONGENITAL HYPOTHYROIDISM

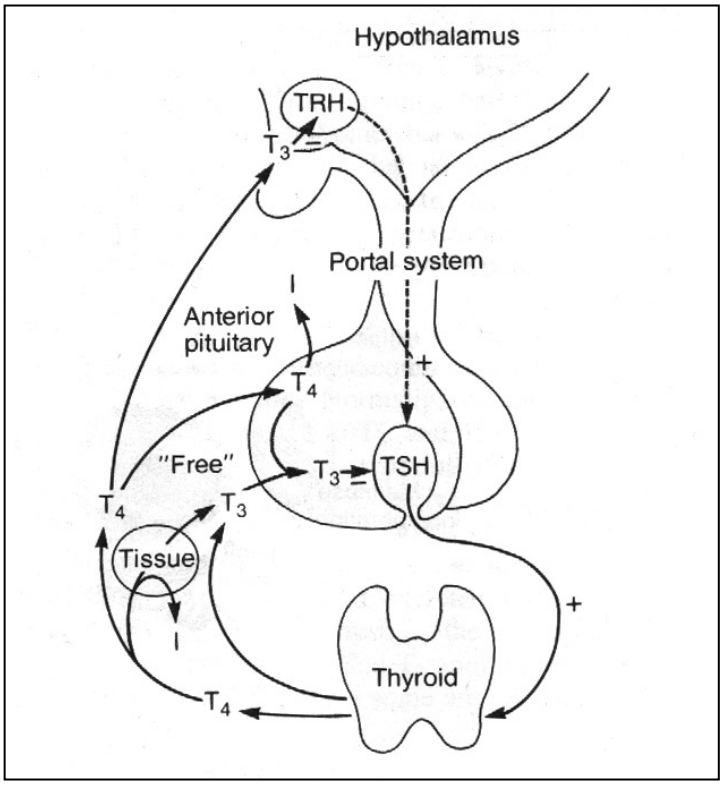
What is Congenital Hypothyroidism (CH) ?

Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation in children. According to the Philippine NBS data, (December 2013) 1 out of 2,733 screened newborns has CH. The most common etiology of CH is thyroid dysgenesis (TD): absent thyroid, ectopic or hypoplastic thyroid. In rare cases, CH results from mutations in the genes that control thyroid gland development including thyroid transcription factor (TTF-2) and paired box-8 protein (PAX-8). Rapid detection by newborn screening, prompt confirmatory testing and Levothyroxine administration can prevent severe mental retardation and impaired growth due to CH.

Pathophysiology

Normal thyroid hormone levels in the body are maintained by a feedback mechanism involving the hypothalmus, pituitary and thyroid gland. The hypothalamus senses low circulating levels of thyroid hormone (T3 and T4) and responds by releasing thyrotropin releasing hormone (TRH). TRH stimulates the anterior pituitary to produce thyroid stimulating hormone (TSH). TSH, in turn, stimulates the thyroid gland to produce thyroid hormone until levels in the blood return to normal. Normal thyroid hormone levels exert a negative feedback to the hypothalamus and the anterior pituitary, thus controlling the release of both TRH from hypothalamus and TSH from anterior pituitary gland. When the thyroid gland does not produce enough T4 and T3, the pituitary gland compensates by producing high levels of TSH. This biochemical profile of low T4 level and high TSH is a pattern consistent with Primary CH. Having the correct level of thyroid hormone in the body is important, especially in the first two years of life, because it ensures normal growth and normal development of the brain, bones and nervous system.

The hypothalamic-pituitary-thyroid axis (HPT axis)



CONGENITAL HYPOTHYROIDISM

Clinical Features

Signs and symptoms of hypothyroidism:
- Decreased activity
- Large anterior fontanelle
- Poor feeding
- poor weight gain
- Small stature or poor growth
- Prolonged Jaundice
- Decreased stooling or constipation
- Hypotonia
- Hoarse cry or weak cry
- Developmental delay

Some physical signs of hypothyroidism that may or may not be present at birth:
- Coarse facial features
- Macroglossia
- Large fontanelles
- Umbilical hernia
- Mottled, cool, and dry skin
- Pallor
- Myxedema
- Goiter

Diagnosis

Newborn screening for primary CH is done by determining the thyroid stimulating hormone (TSH) level on a dried blood spot. If the TSH is significantly elevated, this signifies that the baby is at risk for CH and therefore needs confirmatory thyroid tests. An elevated serum TSH and a low serum FT4 confirms hypothyroidism. Thyroid imaging (thyroid scan or ultrasound) is recommended to document etiology of CH.

Treatment and Monitoring

Immediate diagnosis and treatment of congenital hypothyroidism in the neonatal period is critical to normal brain development and physical growth. Treatment started within the first two weeks of life usually prevents neurodevelopmental delays. Recommended treatment is the lifetime daily administration of Levothyroxine. Only the tablet form of Levothyroxine is currently approved for therapeutic use. The tablets should be crushed, mixed with a few milliliters of water, and fed to the infant directly into the mouth. It is not recommended that Levothyroxine be mixed with soy formula or with formula containing iron, as these interfere with absorption of the medication**.** Thyroid hormone replacement and medical monitoring are required for life.

Children with congenital hypothyroidism should be monitored clinically and biochemically. Clinical parameters should include linear growth, weight gain, head circumference, developmental progression, and overall well-being. Serum T4 or FT4 and TSH should be monitored at regular intervals. The following is the recommendation of the American Academy of Pediatrics

- at 2 and 4 weeks after initiation of T4 treatment
- every 1 to 2 months during the first 6 months of life
- every 3 to 4 months between 6 months and 3 years of age
- every 6 to 12 months thereafter until growth is completed
- after 4 weeks if medication is adjusted
- at more frequent intervals when compliance is in question or abnormal values are obtained.

However, these guidelines on biochemical parameters may be modified by the specialist depending on the clinical status of the patient.

Such evaluations are especially important in children whose treatment was delayed beyond 1 month of life, or in patients whose treatment is inconsistent (non-compliance).

Prognosis

Early diagnosis and optimal treatment of congenital hypothyroidism prevents severe mental retardation, neurologic complications and physical delays. Even with early treatment, some children may demonstrate mild delays in areas such as reading comprehension and arithmetic. Although continued improvement in IQ has been documented in treated patients through adolescence, some cognitive problems may persist. These may include problems in visuospatial, language, and fine motor function. Defects in memory and attention have been reported .

FATTY ACID OXIDATION DISORDERS [FAOD]

FAOD includes:

Medium chain acyl co-A dehydrogenase deficiency (MCAD)
Very long chain acyl Co- A dehydrogenase deficiency (VLCAD)
Long chain hydroxyacyl co-A dehydrogenase deficiency (LCHAD)
Trifunctional protein deficiency (TFI)

What are FAOD?

FAOD are a group of autosomal recessive disorders caused by the deficiency or absence of any of the enzymes needed for beta-oxidation. Children born with this condition appear normal at birth but untreated patients may present with low blood sugar which can lead to seizures, coma and death. One type of FAOD, VLCAD (or very long chain acyl-CoA dehydrogenase deficiency) may present with cardiomyopathy and increased creatine kinase (CK) levels.

Treatment of FAOD

Treatment is through the dietary restriction of fat. VLCAD patients are treated with a special milk formula containing medium chain triglycerides.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent hypoglycemia.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Monitor glucose levels. For patients with VLCAD, collect samples for serum CK. May request for other investigations (i.e. CBC, Blood gas) as needed. May give fluid boluses if patient requires.
d. Start D10% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Monitor input and output strictly (q6 hours). Check for the color of urine.

If unwell and is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with a high glucose formula
b. Insert IV access. Monitor glucose levels. For patients with VLCAD, collect samples for serum CK. May request for other investigations (i.e. CBC, Blood gas) as needed. May give fluid boluses if patient requires.
c. Start D10% 0.3 NaCl at 5-10 cc/hr.
d. Monitor input and output strictly (q6 hours). Check for the color of urine.

*Patients with VLCAD may have rhabdomyolysis. Monitor CK levels and hydrate adequately. If CK levels continually rise, hemodialysis may be indicated.

* Inform metabolic doctor on call for further guidance regarding on-going management.

GALACTOSEMIA

What are Galactosemia?

Galactosemia is a rare genetic metabolic disorder that is inherited in an autosomal recessive manner. It is an inborn error of carbohydrate metabolism characterized by elevated levels of galactose and its metabolites due to enzyme deficiencies involved in its metabolism. Galactose is the sugar found mainly in milk and dairy products. It is also produced by the body. Milk contains a sugar called lactose, and during digestion, lactose is broken down into the sugars glucose and galactose. Glucose can immediately be used as a source of energy by the body, but galactose needs to be further broken down before it can be utilized. The birth incidence of classic galactosemia is about 1 per 47,000 in the Caucasian population. The Philippine NBS data as of December 2013 gives a prevalence of 1 : 33 645.

Pathophysiology

The galactose metabolic pathway with multiple enzymatic steps is shown. The enzymes allow the subsequent conversion of galactose to galactose-1-phosphate by GALK (1); galactose-1-phosphate and uridine diphosphate glucose (UDP glucose) to glucose-1-phosphate and UDP-galactose by GALT (2) and the interconversion of UDP-glucose and UDP-galactose by GALE (3). Children with galactosemia have very little or entirely lack an enzyme that helps the body break down galactose. There are three different enzyme problems that can lead to galactosemia. In the first type or classic galactosemia, the enzyme that is reduced or missing is called galactose-1-phosphate uridyl transferase (GALT). The GALT enzyme enables the body to break down galactose into glucose. The second type of galactosemia is due to a deficiency in uridine diphosphate galactose 4-epimerase (GALE). Its severe type clinically resembles classic galactosemia. The third type, is due to a deficiency in galactokinase (GALK), and presents primarily as cataracts in untreated patients.

Clinical Features

Patients can present with feeding problems, failure to thrive, hepatocellular damage, bleeding, and sepsis in untreated infants. In approximately 10% of individuals, cataracts are present. Failure to thrive is the most common initial clinical symptom of classic galactosemia. Vomiting or diarrhea usually begins within a few days of milk ingestion. Jaundice of intrinsic liver disease may be accentuated by the severe hemolysis occurring in some patients. Cataracts have been observed within a few days of birth. There appears to be a high frequency of neonatal death due to E. coli sepsis in patients with classic galactosemia.

The association of jaundice and hemorrhagic diathesis in the first 2 weeks of life is a clinical presentation in which galactosemia must be considered. Coagulopathy may also be present in galactosemia with little evidence of liver disease. Galactosemia also causes learning and language problems in children, bone mineral density problems and ovarian failure in girls.

Treatment and Monitoring

Dietary elimination of milk and milk products containing lactose is the treatment for all types of galactosemia. There is no chemical or drug substitute for the missing enzyme at this time. An infant diagnosed with galactosemia will have to be on a soy-based formula. Dietary management under the close supervision of a metabolic dietician and a metabolic doctor is a must. Regular monitoring of blood galactose levels and regular evaluation by the genetic metabolic team is important for optimal treatment.

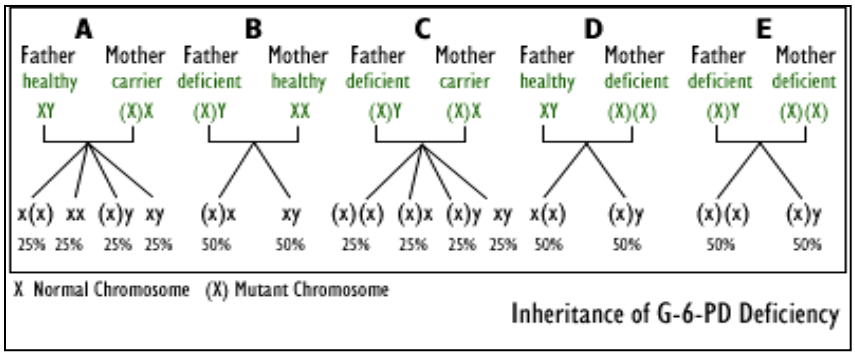
Prognosis

Despite an early galactose-free diet, long-term complications have been noted in older children and adults with classic galactosemia because of endogenous galactose production. These include speech problems, poor intellectual function, neurologic deficits (predominantly extrapyramidal findings with ataxia), and ovarian failure in females. Thus, the need for regular monitoring and evaluation is important.

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

What is G6PD?

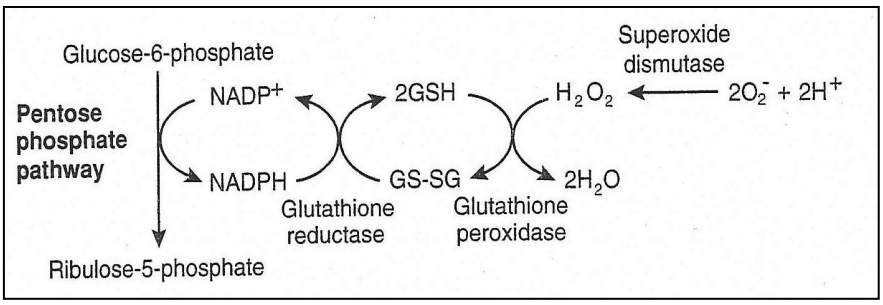
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an enzyme defect affecting around 400 million people worldwide.[5] According to the Philippine NBS data as of December 2013, 1 out of 55 screened newborns have G6PD deficiency.[4] G6PD-deficiency is an X-linked disorder found in both sexes but more males are affected. Female carriers are asymptomatic.



(X)Y – Deficient, Symptomatic
(X)(X) – Deficient, Symptomatic
(X)X – Carrier

PATHOPHYSIOLOGY

G6PD is an enzyme that is present in all cells, but is much valued in red blood cells (RBCs). G6PD is needed for the first step in the Hexose Monophosphate Pathway (HMP). The pathway produces the reduced nicotinamide adenine dinucleotide phosphate (NADPH) that functions as an electron donor in maintaining glutathione in its reduced form (GSH). GSH serves as an antioxidant that protects the cells against oxidative damage. The HMP is the only source of NADPH in RBCs, thus the deleterious effect of G6PD deficiency in RBCs exposed to oxidative stress. Such oxidative stress is brought about by food products, drugs, chemical compounds, and infection. A short list of these agents is available on the succeeding pages.



CLINICAL FEATURES

The most common clinical manifestation of G6PD deficiency is hemolytic anemia induced by various oxidative stresses as mentioned above. The patient presents sudden onset of tea-colored urine, jaundice and pallor. Hereditary nonspherocytic hemolytic anemia may also occur in patients with severe G6PD deficiency. In neonates, G6PD deficiency may present with prolonged jaundice which is attributed to impaired liver function as supposed to hemolysis. The dreaded effect of neonatal jaundice is kernicterus or the deposition of bilirubin (product of hemoglobin catabolism) which causes permanent damage to the brain or death. Other associated disorders to G6PD deficiency are decreased RBC lifespan and cataract formation. Although there is a high prevalence of G6PD deficiency, there are only few severe cases of hemolysis that has been documented and most of them are foreign reports.

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

DIAGNOSIS

The currently used method in the diagnosis of G6PD deficiency is the spot fluorescence test as part of the newborn screening panel. Screening-positive patients should immediately undergo confirmatory testing based on estimation of enzyme activity by quantitative analysis of the rate of NADPH production from NADP. DNA analysis is already available but is not used as a diagnostic method.

MANAGEMENT

There is no cure for G6PD deficiency, but the main goal in the management is avoidance of oxidative insults and blood transfusions for acute hemolytic crisis. Confirmed cases may also be referred to a specialist in Pediatric Hematology for assessment and advice.

PROGNOSIS

Most G6PD-deficient patients live a normal life without the clinical features as indicated above. Since there is no way of telling who will develop hemolytic crisis, avoidance of oxidative stress and physician consult are advised if with febrile illness.

PATIENT EDUCATION

Parents should be educated regarding their child's disorder, specifically the drugs and food that cause oxidative stress, and thus should be avoided. It is also important to emphasize that infection is a common cause of hemolytic crisis in G6PD-deficient patients, hence all affected patients should see their doctor during febrile illness for management. Parents are also advised to mention to their physicians that the patient have G6PD deficiency during consults. As this is an inheritable disease, X-linked, genetic counseling should be done.

References and further reading materials:

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Reddy BM and Tripathy V, Present status of understanding on the G6PD deficiency and natural selection. J Postgrad Med. 2007 July;193-2002.

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

FOODS, DRINKS AND CHEMICALS TO BE AVOIDED IN G6PD DEFICIENCY

I. DRUGS TO BE AVOIDED	
Generic Name	**Common Brand Names**
A. . Antibacterial	
**Nalidixic acid*	
Nitrofuran 1. nitrofurantoin 2. furazolidone 3. nitrofurazone / nitrofural	Macrodantin Diafuran, Diapectolin, Furoxone Furacin
**P- aminosalicylic acid*	
B. Analgesic/ Antipyretic	
**Acetanilid*	
C. Antihelmentic	
**B-naphthol*	
**Niridazole*	
**Stibophan*	
D. Sulfonamides and Sulphones	
Dapsone	Lepravir
**Glucosulphone sodium*	
Glyburide/ Glibenclamide	Euglucon Gluban Lodulce Orabetic
**Mafenide acetate*	
**Salicylazosulphapyridine/ Sulfasalazine*	
Stibophen	(2-(2-Oxido-3,5-Disulphonatophenoxy)-1,3,2,Benzodioxastibole-4-6-Disulphonate)
Sulphacetamide/ Sulfacetamide	Cetapred Sensocet
**Sulphadimidine*	
**Sulphafurazone*	
Sulphamethazole/ Sulfamethazole	Bacidal Bactille Forte Bactrim Bacxal DLI Cotrimoxazole Forteprim Globaxol Pharex Cotrimoxazole Ritemed Cotrimoxazole Septrin Trim S
Sulphanilamide/ Sulfanilamide	
Sulphapyridine	
**Sulphoxone/ Sulfoxone*	
Sulfasalazine, Salazosulfapyridine	Salazopyrin
E. Antimalarials	
Chloroquine	Aralen Chlorofoz
**Pamaquine*	
Primaquine	
Pentaquine	
F. Miscellaneous	
Acetylphenylhydrazine	
Dimercaprol	
Futamide	
Isobutyl nitrate	
Mepacrine	
Phenazopyridine	Azomir
Probenecid	
Thiazolesulfone	
Urate oxidase/ Rasburicase	
II. CHEMICALS TO BE AVOIDED	
Methylene Blue	
Arsine	
Phenylhydrazine	
Toluidine blue	
Trinitrotoluene	
Aniline dyes	
III. FOOD AND DRINKS TO BE AVOIDED	
Fava beans	Dingdong nuts, Mr. Bean
Red wine	
Legumes	Abitsuelas, Garbanzos, Kadyos, Munggo
Blueberry	
Soya food	Taho, Tokwa, Soy Sauce
Tonic water	
Bitter melon / ampalaya	
IV. AT IBA PA	
Menthol	Alaxan Gel Ben-gay Efficascent Oil
	Listerine mouthwash Listerine Pocketpacks Megascent Oil Mentopas Medicated Plaster Omega Pain Killer
Camphor	
Naphthalene	Moth balls
Henna	
Herbs	Cattle gallstone bezoar Honeysuckle flower Chimonanathus flower 100% pearl powder Figwortflower Acalypha indica
V. DRUGS SAFE TO TAKE IN THERAPEUTIC DOSES	
Acetaminophen	Paracetamol, tylenol
Acetophenetidin/ phenacin	
Aspirin/ Acetylsalicylic acid	Alka-seltzer Aspilets Cor-80 Cortal
Ascorbic acid	
Chloramphenicol	Chlormycetin Chloro-S Chlorsig Klorfen Oliphenicol Optomycin Pediachlor Penachlor Speradex
Ciprofloxacin	Ciprobay Clpromax Cipromet Qinosyn-500 Quilox Xipro
Diphenhydramine	
Isoniazid	
Phenytoin	
Quinidine	
**Vitamin K analogues/ Phytomenadione	Hema-K Konakion MM Phil Pharmawealth/ Atlantic Phytomenadione

**Not Available in the Philippines*

***Should be water soluble*

GLUTARIC ACIDURIA TYPE 1 [GA1]

What is GA1?

GA1 is an autosomal recessive disorder caused by the deficiency or absence of the enzyme glutaryl-CoA dehydrogenase. This enzyme breaks down the amino acids lysine and tryptophan which are important precursors of glutaric acid. Deficiency of the enzyme eventually leads to the accumulation of glutaric acid which causes the signs and symptoms such as macrocephaly, seizures, dystonic movements, spasms of the muscles, coma and death.

Treatment of GA1

Treatment is through the dietary restriction of lysine and tryptophan. Patients are given a special milk formula. Carnitine supplementation at 100mg/kg/day is also given.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery, vaccination and severe infection. The goal of treatment is to reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Start IV Carnitine (100mg/kg/day) q6 hours
f. Monitor input and output strictly (q6 hours)

If unwell but is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with GA1 formula or protein free formula
b. Insert IV access. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
c. Start D12.5% 0.3 NaCl at 5-10 cc/hr.
d. Start IV Carnitine (100mg/kg/day) q6 hours
e. Monitor input and output strictly (q6 hours)

* Children should not be protein restricted for longer than necessary (24-48 hours).
* Co-management with a neurologist is indicated to control the dystonia.
* Inform metabolic doctor on call for further guidance regarding on-going management.

GLUTARIC ACIDURIA TYPE II [GA2]

What is GA2?

Glutaric Aciduria Type II is an autosomal recessive disorder caused by the deficiency or absence of either the electron transfer flavoprotein and/or the ETF-ubiquinone oxidoreductase enzyme needed for the breakdown of amino acids and fats. Children born with this condition may remain asymptomatic until later in life but some babies may present with vomiting, acidosis and low blood sugar which can lead to seizures, coma and death.

Treatment of GA2

Treatment is through the dietary restriction of protein and fat. Riboflavin supplementation at 150 mg/day has also been effective. Carnitine may also be given.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Monitor glucose levels. May request for other investigations (i.e. CBC, blood gas, kidney function) as needed. May give fluid boluses if patient requires.
d. Start D10% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Monitor input and output strictly (q6 hours).

If unwell and is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with a high glucose formula
b. Insert IV access. Monitor glucose levels. May request for other investigations (i.e. CBC, blood gas, kidney function) as needed. May give fluid boluses if patient requires.
c. Start D10% 0.3 NaCl at 5-10 cc/hr.
d. Monitor input and output strictly (q6 hours).

* Inform metabolic doctor on call for further guidance regarding on-going management.

HOMOCYSTINURIA [HCY]

What is HCY?

Homocystinuria is an autosomal recessive disorder caused by the deficiency or absence of the cystathionine beta-synthase (CBS) enzyme. Children born with this condition appear normal at birth but during childhood untreated children may present with a marfanoid appearance, lens dislocation, mental retardation, scoliosis and thrombus formation.

Treatment of HCY

Treatment is through the dietary restriction of protein and the supplementation of formula lacking methionine. Vitamin B6, folic acid and betaine are also given.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as SURGERY and severe infection. The goal of treatment is to reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Collect samples for methionine and homocystine levels (contact the Biochemical Genetic Laboratory NIH). May request for other investigations (i.e. CBC, Blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance especially if the patient will undergo surgery.
e. Make sure that the patient is well hydrated. Monitor input and output strictly (q6 hours)
f. Start betaine, folic acid and vitamin B6

If unwell but is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with HCY formula to run at maintenance rate
b. Insert IV access. Collect samples for methionine and homocystine level (contact the Biochemical Genetics Laboratory, NIH). May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
c. Start D12.5% 0.3 NaCl at 5-10 cc/hr. Make sure that the patient is well hydrated especially if he will undergo surgery. Monitor input and output strictly (q6 hours)
d. Start betaine, folic acid and vitamin B6

*Children should not be protein restricted for longer than necessary (24-48 hours).

* Inform metabolic doctor on call for further guidance regarding on-going management.

METHIONINE ADENOSINE TRANSFERASE DEFICIENCY

What is Methionine Adenosine Transferase Deficiency?

Methionine Adenosine Transferase (MAT) Deficiency is an autosomal recessive disorder caused by the deficiency or absence of the methionine adenosine transferase enzyme needed for the breakdown of methionine. Children born with this condition appear normal at birth but untreated patients may present with tremors, seizures, dystonia and myelination disorders.

Treatment of MAT Deficiency

Treatment is through the dietary restriction of protein. S-adenosylmethionine administration has been found to be effective in neurologic development.

*Should patients become unwell, please call metabolic doctor on call for further guidance.

MULTIPLE CARBOXYLASE DEFICIENCY

What is Multiple Carboxylase Deficiency?

Multiple carboxylase deficiency is an autosomal recessive disorder caused by the deficiency or absence of the enzyme holocarboxylase synthetase. This enzyme is needed to add biotin to the carboxylase enzymes for them to work properly. Untreated children born with this condition may present with lethargy, coma, seizures, hyptonia, vomiting, alopecia, skin rash. Patients may also present with hyperammonemia, ketosis and severe metabolic acidosis.

Treatment of Multiple Carboxylase Deficiency

Treatment is through biotin supplementation. The clinical response to treatment is dramatic. Ketosis and acidosis disappear along with hyperammonemia, lethargy, hypotonia and ataxia. The dermatological effects of the disorder are likewise reversed.

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MAPLE SYRUP URINE DISEASE [MSUD]

What is MSUD?

Maple syrup urine disease is an autosomal recessive disorder caused by the deficiency or absence of the branched-chain ketoacid dehydrogenase (BCKAD) enzyme. Patients may present with poor suck, lethargy, vomiting, irritability and seizures. If left untreated, patients may have brain edema, spasticity and eventual coma. This leads to brain damage and possible mental retardation.

Treatment of MSUD

Treatment is through the dietary restriction of protein and the supplementation of formula lacking leucine, valine and isoleucine.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to lower down the levels of leucine, isoleucine and valine, reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Collect samples for leucine level, plasma amino acids, blood glucose and urine ketones. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Start intralipid at 1g/kg/24 hours.
f. Monitor input and output strictly (q6 hours)

If unwell but is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with BCAD formula to run at maintenance rate
b. May give valine at 50mg/kg/day divided into 6 doses and isoleucine 30mg/kg/day divided into 6 doses
c. Insert IV access. Collect samples for leucine level, plasma amino acids, blood glucose and urine ketones. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at 5-10 cc/hr.
e. Monitor input and output strictly (q6 hours)

*Children should not be protein restricted for longer than necessary (24-48 hours).

*If patient does not improve with the initial management (within 12 hours), hemodialysis may be indicated. Monitor patient clinically, the necessity of hemodialysis will depend on patient's clinical status.

* Inform metabolic doctor on call for further guidance regarding on-going management.

ORGANIC ACIDURIAS

What are Organic Acidurias?

Organic acidurias are a group of autosomal recessive disorder caused by the deficiency or absence of any of the enzymes needed for the breakdown of some proteins. They derive their names from the substance that accumulates proximal to the block in the pathway. They are the following:

Propionic aciduria (PA) – due to a deficiency of propionyl-CoA carboxylase
Methylmalonic aciduria (MMA) – due to a defiency of methymalonyl-CoA mutase
Isovaleric aciduria (IVA) – due to a deficiency of isovaleryl-CoA dehydrogenase

Untreated children with this condition may present with vomiting, irritability, drowsiness, rapid breathing and coma. Patients with propionic aciduria and isovaleric aciduria may also have hyperammonemia. As a result, untreated children may have encephalopathy, mental retardation or death.

Treatment of Organic Acidurias

Treatment is through the dietary restriction of protein. Children may be given a special milk formula that is protein free. Carnitine and/or glycine are also prescribed.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

if unwell and cannot tolerate oral intake:

a. Nothing per orem except medications
b. Ensure patient's airway is secure
c. Insert IV access. Collect samples for ammonia, blood gas, electrolytes and urine ketones. May request for other investigations (i.e. CBC, urine organic acids) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Give Carnitine IV (100mg/kg/day) q6 hours. For children with IVA, may give glycine (150mg/kg/day) q8 hours.
f. Monitor input and output strictly (q6 hours)

If unwell and is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with protein free formula
b. Insert IV access. Collect samples for ammonia, blood gas, electrolytes and urine ketones. May request for other investigations (i.e. CBC urine organic acids) as needed. May give fluid boluses if patient requires.
c. Start D12.5% 0.3 NaCl at 5-10 cc/hr.
d. Give Carnitine IV (100mg/kg/day) q6 hours. For children with IVA, may give glycine (150mg/kg/day) q8 hours.
e. Monitor input and output strictly (q6 hours)

*Patients with PA and IVA may have hyperammonemia. Monitor ammonia levels every 4 hours. If ammonia remains above 200mmol/L for three consecutive collections, medical treatment or hemodialysis may be indicated.

* Inform metabolic doctor on call for further guidance regarding on-going management.

PHENYLKETONURIA

What is PKU?

Phenylketonuria is an autosomal recessive disorder caused by the deficiency or absence of the phenylalanine hydroxylase (PAH) enzyme. At birth, children with PKU may seem normal. However, they may present with developmental delay. Untreated children may also have decreased attention span, mental retardation, irritability, seizures, hyperactivity and behavioral problems. The increased levels of phenylalanine in the brain may cause brain damage.

Treatment of PKU

Treatment is through the dietary restriction of protein and the supplementation of formula lacking phenylalanine. Patients are also advised to avoid taking aspartame found in artificial sweeteners because aspartame contains high levels of phenylalanine.

Preliminary / Initial Management During Metabolic Crises

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Collect samples for phenylalnine levels. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Start Intralipid at 1g/kg/day
f. Monitor input and output strictly (q6 hours)

If unwell but is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with PKU formula to run at maintenance rate
b. Insert IV access. Collect samples for phenylalanine levels. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
c. Start D12.5% 0.3 NaCl at 5-10 cc/hr.
d. Monitor input and output strictly (q6 hours)

*Children should not be protein restricted for longer than necessary (24-48 hours).

* Inform metabolic doctor on call for further guidance regarding on-going management.

THALASSEMIAS AND HEMOGLOBINOPATHIES

What are Thalassemias and Hemoglobinopathies?

Thalassemias are characterized by a decreased production in the either the α or β globin chains. They are grouped into α and β thalassemias. The imbalance in the production of globin chain results in a haemolytic anemia or precipitation of the red cells in the bone marrow or a process known as ineffective erythropoiesis.

Hemoglobinopathies on the other hand are structural abnormalities and are usually due to a single amino acid substitution.

Both disorders exhibit unique geographical distribution. HbS, HbSC, HbS/β thalassemia or sickle cell disease is typically common in Africa, Saudi Arabia, India and in the Americas. HbE is almost exclusively from South East Asia.

ALPHA THALASSEMIAS

The alpha thalassemias are probably the more common of the 2 thalassemias. Most alpha thalassemia mutations are due to deletions of which more than 50 have been identified. The 2 most common deletions are the ---SEA seen in South East Asia and the MED-1 in the Mediterranean. Alpha thalassemia may result from the loss of the alpha globin gene. There are 4 alpha globin gene so the loss may be from one to four of the gene. The clinical symptomatology will depend on the number of gene deletions. The loss of 4 genes results in **hydrops fetalis** which is fatal in utero. Loss of 3 genes indicates **HbH disease** which may manifest later in childhood as moderately severe anemia. Iron overload becomes a major problem when these patients reach puberty and adulthood. Loss of 2 genes (trait) or 1 (silent carrier) may result in mild anemia and these two are clinically insignificant. South East Asians may have all 4 types.

The percentage of haemoglobin Bart's in the cord blood may indicate the number of alpha gene loss. If the percentage is < 10% then the infant may have 1 or 2 gene loss. If the amount of Bart's is > 20-25% then it may indicate a more severe form of alpha thalassemia such as HbH disease. Non deletional form of HbH disease such as HbH Constant Spring are clinically more severe.

Clinical Signs of Alpha Thalassemia

Loss of 1 or 2 α genes often asymptomatic with mild anemia at the most. The smear will show microcytosis which is often mistaken for iron deficiency anemia. Patients who do not respond to iron therapy for their anemia should be worked up for possible thalassemias. Parents should be assured that their children will be symptom free but they should also be made aware that the trait may run in their family.

If the Bart's is 20-25% and the infant is either South East Asian or from the Mediterranean then HbH should strongly be considered and the family referred to a haematologist.

HbH disease is due to deletion of 3 alpha genes resulting in the formation of beta tetramers (β4). Clinically this is classified as a form of **thalassemia intermedia**. A non deletional form of HbH disease such as **HbH Constant Spring** is seen when 2 alpha gene deletion such the ---SEA deletion is seen in conjunction with an α gene mutation such as the Constant Spring mutation. Patients usually exhibit a more severe form of anemia requiring regular transfusions early in childhood resulting in iron overload later on in life. These patients will require special care.

Patients with non deletional form of HbH disease develop symptoms at an earlier age with more severe anemia, growth stunting, hepatosplenomegaly, dysmorphic facial features and require more transfusions than the deletional forms.

BETA THALASSEMIAS

In contrast to α thalassemias, the vast majority of mutations in β thalassemias are non deletional. Beta Thalassemia mutations may result in total absence of beta chain production (β°) or partial reduction of the chain (β+). Decreased haemoglobin production leads to microcytosis, ineffective erythropoiesis and skeletal changes. A presumptive diagnosis of β thalssemia in the newborn is made if the HbF is the sole haemoglobin with absent HbA .

Clinical features may vary depending on the complete or partial absence of the beta chain. Beta thalassemia major patients (β°β°) are transfusion dependent as early as the late infancy period while thalassemia intermedia (β°β+) or (β+β+) has less severe anemia and require fewer transfusions. Children heterozygous for a normal and a beta thalassemia gene will have very mild anemia, microcytosis, and slight splenomegaly. Transfusion is usually not required. They are often confused with iron deficiency anemia.

There are individuals who are compound heterozygote for HgB E and β° thalassemia. HbE/β thalssemia presents in infancy as variably severe anemia with clinical phenotype ranging from complete lack of symptoms to transfusion dependence. Osteoporosis, iron overload, growth failure, pulmonary hypertension ae commonly reported in both transfused and nontransfused patients. Patients presenting with thalassemia intermedia phenotype during childhood often become transfusion dependent as adults due to worsening anemia and fatigue. They may eventually develop iron overload and will likely succumb to cardiac failure later in life.

Patients with beta thalassemia major are best managed in a specialized hospital as they will need regular transfusions and iron chelation. Those with the minor form of the disease will not need special care. Intermedia patients may need specialized care later in childhood as iron overload may present later in life so inadvertent and prolonged use of iron are discouraged in these patients.

HEMOGLOBIN E

Hgb E is the most common hemoglobinopathy variant in South East Asia. The βE chain is synthesized at a reduced rate leading to an imbalance in the globin chains.

HgbE traits do not exhibit clinical disease. There is slight anemia with microcytosis. Target cells are seen in the smears. The Hb E is > 30%.

Homozygous HbE individuals likewise are asymptomatic but the haemoglobin level may be lower than the trait. The red cell indices are likewise low. The two conditions do not warrant special care.

In regions where there is a high incidence of α and β thalassemias such as the Philippines, HbE may be coinherited with these disorders. HbE with HbH may result in moderately severe thalassemic findings similar to thalassemia intermedia.. HbE level is between 10-15%.

HbE/β° as mentioned previously may behave as thalassemia major and will need to be managed in a specialty center.

OTHER HEMOGLOBINOPATHIES

Sickle cell disease patients have predominant HbS. They are most common in Africa, Saudi Arabia and the United States The affected infants are usually normal at birth but develop anemia later when the HbS concentration increases and the HbF decreases. These patients are particularly susceptible encapsulated bacterial infections such as Streptococcus pneumonia, H. influenza, Staphylococcus aureus, and Salmonella. Prophylactic penicillin should be started early in infancy once diagnosis is made.

Heterozygotes (Hb AS) are usually asymptomatic and are referred to as trait.

References:

Hoppe, C., Newborn Screening for Non- Sickling Hemoglobinopathy, ASH Education Book, 2009

Hoyer, J. 79 Hemoglobinopathies, Annual Meeting of the American Society of Clinical Pathologists, 2011

Welch, S. Hemoglobinopathies and Thalassemias, Clinical Lab News, Oct 2009, Vol 15

Georgia Newborn Screening Manual for Metabolic Diseases and Hemoglobinopathies, Pp 38-61

THALASSEMIAS AND HEMOGLOBINOPATHIES (Hemoglobin E)

The baby's newborn screening test identified him/her as a carrier of Hemoglobin E, also referred to as **Hemoglobin E Trait** or **Hb AE**.

Clinical Expectations for Carriers of Hemoglobin E

Being a carrier of Hemoglobin E will not have an adverse influence on this child's life expectancy. The trait is basically silent and carriers are not more likely to get sick than any other child. In most cases, children are symptom-free and will have normal growth and development, hence do not need special medical care. Rarely, carriers can manifest with mild anemia.

Reproductive Risks

The results indicate that the child is a carrier of the Hemoglobin E. It is important to remember that the trait may be transmitted by the child to his would-be children. Thus, it is extremely important to have his/her future partner screened for the trait as their union may result in a baby with a severe case of thalassemia. Family members of this child may also be at-risk for a hemoglobin disease. Carrier-testing is recommended for parents and other family members.

Carrier Testing Recommendations

Hemoglobinopathy carrier testing can be performed by:

1. CBC to assess MCV

2. Hemoglobin analysis (by Capillary electrophoresis (CE) or High performance liquid chromatography (HPLC).

3. Serum ferritin (to enable interpretation of MCV and hemoglobin analysis).

Important Considerations

• Refrain from giving Iron supplements to the child. Folic acid is recommended.

• Immunizations are not contraindicated for this condition, and may be given as recommended by the Philippine Pediatric Society. It is also recommended that they be given Pneumococcal, Influenza and Haemophilus influenza Type B (HiB) vaccines.

Referral Indications

•To Genetics: Refer parents if they are both carriers, ideally prior to the next pregnancy for a review of reproductive testing options.

•To Hematology: Refer any individual in the family identified to have a hemoglobinopathy to a Hematologist for assessment and management.

Should you have any other concerns, please do not hesitate to contact us through the following numbers: (02) 376-0962; 376-0964. Fax (02) 921-6395. Email: NSC-NIH@upm.edu.ph or the nearest Continuity Clinic:_____

THALASSEMIAS AND HEMOGLOBINOPATHIES (Hemoglobin C)

The child's newborn screening test identified them as a carrier of Hemoglobin C, also referred to as **Hemoglobin C Trait** or **Hb AC**.

Clinical Expectations for Carriers of Hemoglobin C

Being a carrier of Hemoglobin C will not have an adverse influence on this child's life expectancy. The trait is basically silent and carriers are **not** more likely to get sick than any other child. In most cases, children are symptom-free and will have normal growth and development, hence do **not** need special medical care. Rarely, carriers can manifest with mild anemia.

Reproductive Risks

The results indicate that the child is a carrier of the Hemoglobin C. It is important to remember that the trait may be transmitted by the child to his would-be children. Thus, it is extremely important to have his/her future partner screened for the trait as their union may result in a baby with a severe case of hemoglobinopathy. Family members of this child may also be at-risk for a hemoglobin disease. Carrier-testing is recommended for parents and other family members.

Carrier Testing Recommendations

Hemoglobinopathy carrier testing can be performed by:

1. CBC to assess MCV

2. Hemoglobin analysis (by Capillary electrophoresis (CE) or High performance liquid chromatography (HPLC).

3. Serum ferritin (to enable interpretation of MCV and hemoglobin analysis).

Important Considerations

• Refrain from giving Iron supplements to the child. Folic acid is recommended.

• Immunizations are not contraindicated for this condition, and may be given as recommended by the Philippine Pediatric Society. It is also recommended that they be given Pneumococcal, Influenza and Haemophilus influenza Type B (HiB) vaccines.

Referral Indications

•To Genetics: Refer parents if they are both carriers, ideally prior to the next pregnancy for a review of reproductive testing options.

•To Hematology: Refer any individual in the family identified to have a hemoglobinopathy to a Hematologist for assessment and management.

Should you have any other concerns, please do not hesitate to contact us through the following numbers: (02) 376-0962; 376-0964. Fax (02) 921-6395. Email: NSC-NIH@upm.edu.ph or the nearest Continuity Clinic:_____

THALASSEMIAS AND HEMOGLOBINOPATHIES (Hemoglobin D)

The child's newborn screening test identified them as a carrier of Hemoglobin D, also referred to as **Hemoglobin D Trait** or **Hb AD**.

Clinical Expectations for Carriers of Hemoglobin D

Being a carrier of Hemoglobin D will not have an adverse influence on this child's life expectancy. The trait is basically silent and carriers are **not** more likely to get sick than any other child. In most cases, children are symptom-free and will have normal growth and development, hence do **not** need special medical care. Rarely, carriers can manifest with mild anemia.

Reproductive Risks

The results indicate that the child is a carrier of the Hemoglobin D. It is important to remember that the trait may be transmitted by the child to his would-be children. Thus, it is extremely important to have his/her future partner screened for the trait as their union may result in a baby with a severe case of hemoglobinopathy. Family members of this child may also be at-risk for a hemoglobin disease. Carrier-testing is recommended for parents and other family members.

Carrier Testing Recommendations

Hemoglobinopathy carrier testing can be performed by:

1. CBC to assess MCV
2. Hemoglobin analysis (by Capillary electrophoresis (CE) or High performance liquid chromatography (HPLC).
3. Serum ferritin (to enable interpretation of MCV and hemoglobin analysis).

Important Considerations

• Refrain from giving Iron supplements to the child. Folic acid is recommended.

• Immunizations are not contraindicated for this condition, and may be given as recommended by the Philippine Pediatric Society. It is also recommended that they be given Pneumococcal, Influenza and Haemophilus influenza Type B (HiB) vaccines.

Referral Indications

•To Genetics: Refer parents if they are both carriers, ideally prior to the next pregnancy for a review of reproductive testing options.

•To Hematology: Refer any individual in the family identified to have a hemoglobinopathy to a Hematologist for assessment and management.

Should you have any other concerns, please do not hesitate to contact us through the following numbers: (02) 376-0962; 376-0964. Fax (02) 921-6395. Email: NSC-NIH@upm.edu.ph or the nearest Continuity Clinic:_____

THALASSEMIAS AND HEMOGLOBINOPATHIES (Sickle Cell)

The child's newborn screening test identified them as a carrier of Sickle Cell Disease (SCD), also referred to as **Sickle Cell Trait** or **Hb AS**.

Clinical Expectations for Carriers of Sickle Cell Disease

Being a carrier of Hemoglobin S will not have an adverse influence on this child's life expectancy. The trait is basically silent and carriers are **not** more likely to get sick than any other child. In most cases, children are symptom-free and will have normal growth and development, hence do **not** need special medical care. Rarely, carriers can manifest with mild anemia.

Reproductive Risks

The results indicate that the child is a carrier of the Hemoglobin S (Sickle cell Hemoglobin). It is important to remember that the trait may be transmitted by the child to his would-be children. Thus, it is extremely important to have his/her future partner screened for the trait as their union may result in a baby with a severe case of Sickle Cell Disease. Family members of this child may also be at-risk for a hemoglobin disease. Carrier-testing is recommended for parents and other family members.

Carrier Testing Recommendations

Hemoglobinopathy carrier testing can be performed by:

1. CBC to assess MCV
2. Hemoglobin analysis (by Capillary electrophoresis (CE) or High performance liquid chromatography (HPLC).
3. Serum ferritin (to enable interpretation of MCV and hemoglobin analysis).

Important Considerations

• Refrain from giving Iron supplements to the child. Folic acid is recommended.

• Immunizations are not contraindicated for this condition, and may be given as recommended by the Philippine Pediatric Society. It is also recommended that they be given Pneumococcal, Influenza and Haemophilus influenza Type B (HiB) vaccines.

Referral Indications

•To Genetics: Refer parents if they are both carriers, ideally prior to the next pregnancy for a review of reproductive testing options.

•To Hematology: Refer any individual in the family identified to have a hemoglobinopathy to a Hematologist for assessment and management.

Should you have any other concerns, please do not hesitate to contact us through the following numbers: (02) 376-0962; 376-0964. Fax (02) 921-6395. Email: NSC-NIH@upm.edu.ph or the nearest Continuity Clinic:_____

THALASSEMIAS AND HEMOGLOBINOPATHIES (Alpha Thalassemia)

The child's newborn screening test identified them as a carrier of Alpha Thalassemia, also referred to as **Alpha Thalassemia Trait/Minor**.

Clinical Expectations for Carriers of Alpha Thalassemia

Being a carrier of Alpha Thalassemia will not have an adverse influence on this child's life expectancy. The trait is basically silent and carriers are **not** more likely to get sick than any other child. In most cases, children are symptom-free and will have normal growth and development, hence do **not** need special medical care. Rarely, carriers can manifest with mild anemia.

Reproductive Risks

The results indicate that the child is a carrier of Alpha Thalassemia. It is important to remember that the trait may be transmitted by the child to his would-be children. Thus, it is extremely important to have his/her future partner screened for the trait as their union may result in a baby with a severe case of thalassemia. Family members of this child may also be at-risk for a hemoglobin disease. Carrier-testing is recommended for parents and other family members.

Carrier Testing Recommendations

Hemoglobinopathy carrier testing can be performed by:
1. CBC to assess MCV
2. Hemoglobin analysis (by Capillary electrophoresis (CE) or High performance liquid chromatography (HPLC).
3. Serum ferritin (to enable interpretation of MCV and hemoglobin analysis).

Important Considerations

• Refrain from giving Iron supplements to the child. Folic acid is recommended.
• Immunizations are not contraindicated for this condition, and may be given as recommended by the Philippine Pediatric Society. It is also recommended that they be given Pneumococcal, Influenza and Haemophilus influenza Type B (HiB) vaccines.

Referral Indications

•To Genetics: Refer parents if they are both carriers, ideally prior to the next pregnancy for a review of reproductive testing options.
•To Hematology: Refer any individual in the family identified to have a hemoglobinopathy to a Hematologist for assessment and management.

Should you have any other concerns, please do not hesitate to contact us through the following numbers: (02) 376-0962; 376-0964. Fax (02) 921-6395. Email: NSC-NIH@upm.edu.ph or the nearest Continuity Clinic:_____

THALASSEMIAS AND HEMOGLOBINOPATHIES (Beta Thalassemia)

The child's newborn screening test identified them as a carrier of Beta Thalassemia, also referred to as **Beta Thalassemia Trait/Minor**.

Clinical Expectations for Carriers of Beta Thalassemia

Being a carrier of Beta Thalassemia will not have an adverse influence on this child's life expectancy. The trait is basically silent and carriers are **not** more likely to get sick than any other child. In most cases, children are symptom-free and will have normal growth and development, hence do **not** need special medical care. Rarely, carriers can manifest with mild anemia.

Reproductive Risks

The results indicate that the child is a carrier of Beta Thalassemia. It is important to remember that the trait may be transmitted by the child to his would-be children. Thus, it is extremely important to have his/her future partner screened for the trait as their union may result in a baby with a severe case of thalassemia. Family members of this child may also be at-risk for a hemoglobin disease. Carrier-testing is recommended for parents and other family members.

Carrier Testing Recommendations

Hemoglobinopathy carrier testing can be performed by:
1. CBC to assess MCV
2. Hemoglobin analysis (by Capillary electrophoresis (CE) or High performance liquid chromatography (HPLC).
3. Serum ferritin (to enable interpretation of MCV and hemoglobin analysis).

Important Considerations

• Refrain from giving Iron supplements to the child. Folic acid is recommended.
• Immunizations are not contraindicated for this condition, and may be given as recommended by the Philippine Pediatric Society. It is also recommended that they be given Pneumococcal, Influenza and Haemophilus influenza Type B (HiB) vaccines.

Referral Indications

•To Genetics: Refer parents if they are both carriers, ideally prior to the next pregnancy for a review of reproductive testing options.
•To Hematology: Refer any individual in the family identified to have a hemoglobinopathy to a Hematologist for assessment and management.

Should you have any other concerns, please do not hesitate to contact us through the following numbers: (02) 376-0962; 376-0964. Fax (02) 921-6395. Email: NSC-NIH@upm.edu.ph or the nearest Continuity Clinic:_____

TYROSINEMIA TYPE I

What is Tyrosinemia Type I (Hepatorenal tyrosinemia)?

Tyrosinemia Type I is an autosomal recessive disorder caused by the deficiency or absence of the fumarylacetoacetate hydrolase (FAH) enzyme. Children may present with jaundice, diarrhea and bloody stools, failure to thrive, irritability, drowsiness, hepatomegaly and coagulopathy. Some patients may also present with renal problems, pain and paresthesia.

Treatment of Tyrosinemia

Treatment is through the dietary restriction of protein and the supplementation of formula lacking tyrosine. Patients are also given nitisinone (NTBC) which is an inhibitor of p-hydroxyphenylpyruvate dioxygenase as maintenance medication.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, high consumption of protein, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to control level of tyrosine, correct bleeding parameters, reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem except medications
b. Ensure patient's airway is secure
c. Insert IV access. Collect samples for blood glucose, plasma amino acids, liver function tests, coagulation studies and urine succinylacetone. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Start nitisinone (2mg/kg) per orem.
f. Monitor input and output strictly (q6 hours)

If unwell but is able to tolerate oral intake:

a. Insert oro- or nasogastric tube and start continuous feeding with tyrosine free formula to run at maintenance rate
b. Start nitisinone (2mg/kg) per NGT
c. Insert IV access. Collect samples for blood glucose, plasma amino acids, liver function tests, coagulation studies and urine succinylacetone. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at 5-10 cc/hr.
e. Monitor input and output strictly (q6 hours)

*Children should not be protein restricted for longer than necessary (24-48 hours).

* Inform metabolic doctor on call for further guidance regarding on-going management.

UREA CYCLE DEFECTS

UREA CYCLE DEFECTS: Citrullinemia AND Argininosuccinic Aciduria

What are UCDs?

The urea cycle is the main pathway of the body to dispose of excess nitrogen. It allows for the conversion of ammonia into urea that can be excreted into the urine. Citrullinemia and Argininosuccinic Aciduria are inherited in an autosomal recessive manner. Citrullinemia occurs as a result of argininosuccinic synthase deficiency while argininosuccinic aciduria is due to a deficiency of argininosuccinic lyase. Both conditions may manifest with tachypnea, lethargy, vomiting, irritability, seizures, coma and ultimately death if left untreated. The increased levels of ammonia may cause brain damage.

Due to blocks in the urea cycle owing to the enzyme deficiency, patients with UCD have low levels of arginine. This makes arginine an essential amino acid among patients with UCD.

Treatment of UCDs

Treatment is through the dietary restriction of protein and the supplementation of a protein free formula. Sodium benzoate, an ammonia scavenger, is given as well as arginine supplementation.

Preliminary / Initial Management During Metabolic Crises

Metabolic crises may be caused by an excess intake of protein, illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent essential amino acid deficiency.

What to Do:

If unwell and cannot tolerate oral intake:

a. Nothing per orem
b. Ensure patient's airway is secure
c. Insert IV access. Collect samples for serum ammonia. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
d. Start D12.5% 0.3 NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5X the maintenance.
e. Start IV sodium benzoate loading dose (250mg/kg) to run for four hours
f. Start IV arginine loading dose (250mg/kg) to run for four hours
g. Monitor input and output strictly (q6 hours)

I*f unwell but is able to tolerate oral intake:*

a. Insert oro- or nasogastric tube and start continuous feeding with protein free formula to run at maintenance rate
b. Insert IV access. Collect samples for serum ammonia. May request for other investigations (i.e. CBC, blood gas) as needed. May give fluid boluses if patient requires.
c. Start D12.5% 0.3 NaCl at 5-10 cc/hr.
d. Start IV sodium benzoate loading dose (250mg/kg) to run for four hours
e. Start IV arginine loading dose (250mg/kg) to run for four hours
f. Monitor input and output strictly (q6 hours)

*Children should not be protein restricted for longer than necessary (24-48 hours).

*If patient does not improve with the initial management (within 12 hours), hemodialysis may be indicated. Monitor patient clinically, the necessity of hemodialysis will depend on patient's clinical status.

* Inform metabolic doctor on call for further guidance regarding on-going management.