	NEWBORN SCREENING REFERENCE CENTER	
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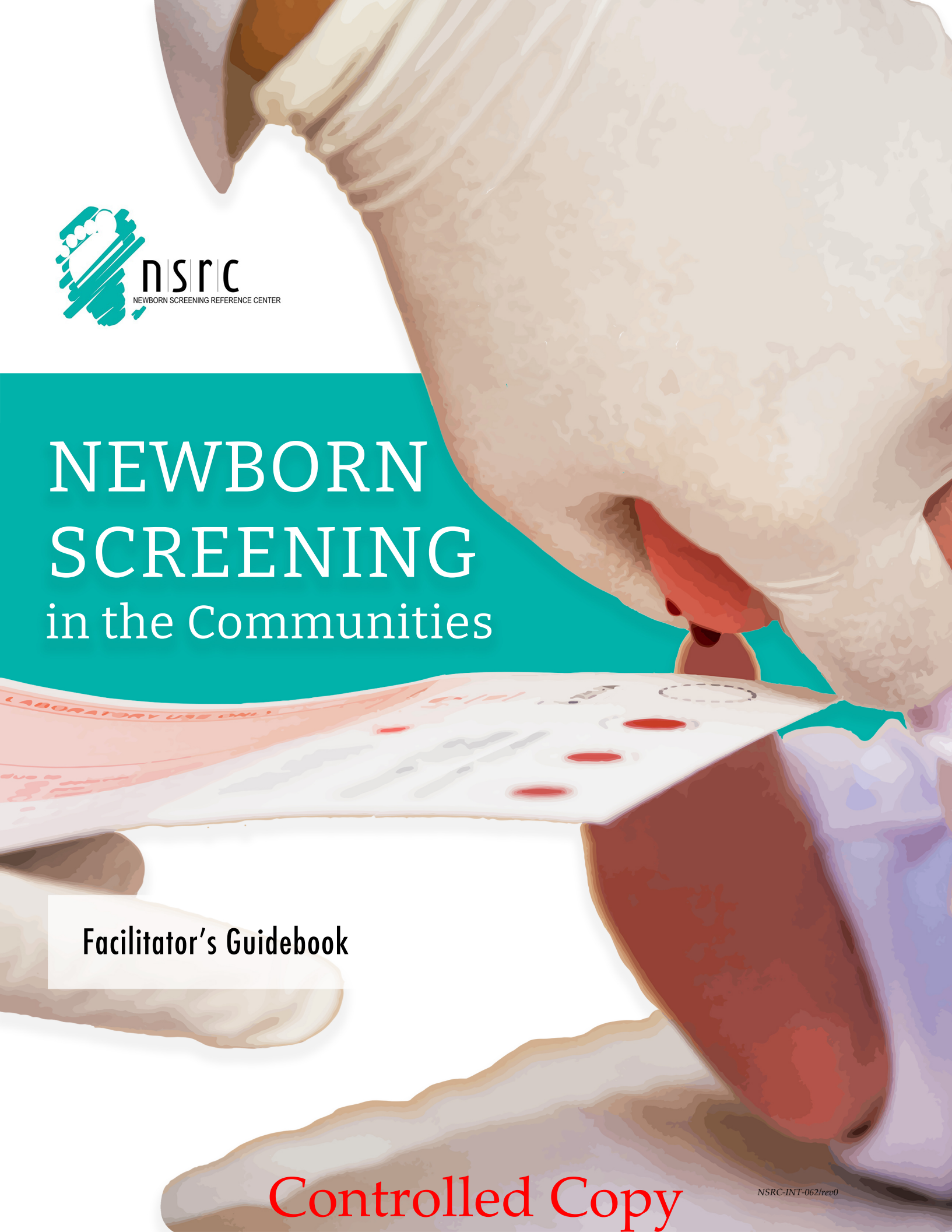

nsrc
NEWBORN SCREENING REFERENCE CENTER

NEWBORN SCREENING
in the Communities

Facilitator's Guidebook

NSRC-INT-062/rev0

PREFACE

The updated Facilitator's Guidebook: Newborn Screening in the Communities is a product of a concerted effort of key newborn screening program implementers to come up with an up-to-date instructional material to facilitate easy teaching and learning process. The need to come up with a ready reference arises due to the evident need to support newborn screening facilitators when organizing and running newborn screening orientations. It standardizes the information to be communicated to all health workers.

This version contains new developments in the program, updated statistics and data, and recommendations on how to conduct the training orientation. This guidebook includes slide presentations, scripts, and additional notes that may aid the facilitator in delivering the presentation. The script is based on the usual lines delivered in previous orientations as well as valuable contributions from the newborn screening pool of speakers and input from the Newborn Screening Centers, Centers for Health Development, and Newborn Screening Continuity Clinics.

There are five sections in this guidebook:

Module 1 contains an overview of the general aspects of the screening program. It describes the history of newborn screening in the Philippines as well as its importance.

Module 2 presents the highlights of RA 9288 (the Newborn Screening Act of 2004) with an emphasis on the role of health workers and its implications on the health facilities in the country.

Module 3 is devoted to the procedures for implementing newborn screening in health facilities. The presentation includes the newborn screening flow of operations.

Elective Module 1 is optional for refresher courses. This module discusses the role of Newborn Screening Continuity Clinics (NBSCCs) in the national newborn screening program.

Elective Module 2 is also an optional course that discusses each of the disorders in the Expanded Newborn Screening Panel, along with their symptoms and treatment. This course is recommended if the need arises based on the training needs of the participants.

Each of the modules have two versions, one for face-to-face trainings, and another for online trainings. Use the module appropriate for your training's mode of delivery. If you want more information about newborn screening, particularly on the conditions included in the expanded newborn screening panel, you may go through the Fact Sheets for Doctors, NCNBSS Manual of Operations, or visit www.newbornscreening.ph for more resources and information.

We hope that using this guidebook will be beneficial to you. Any pertinent information (such as local policies) may be incorporated or updated as appropriate. In order to help you the most, we ask for your feedback while you use this guidebook. Every year, NSRC will update this manual to reflect the most recent information, address persistent issues, and give facilitators further guidance on any crucial aspects of the newborn screening program.

Thank you and stay safe!

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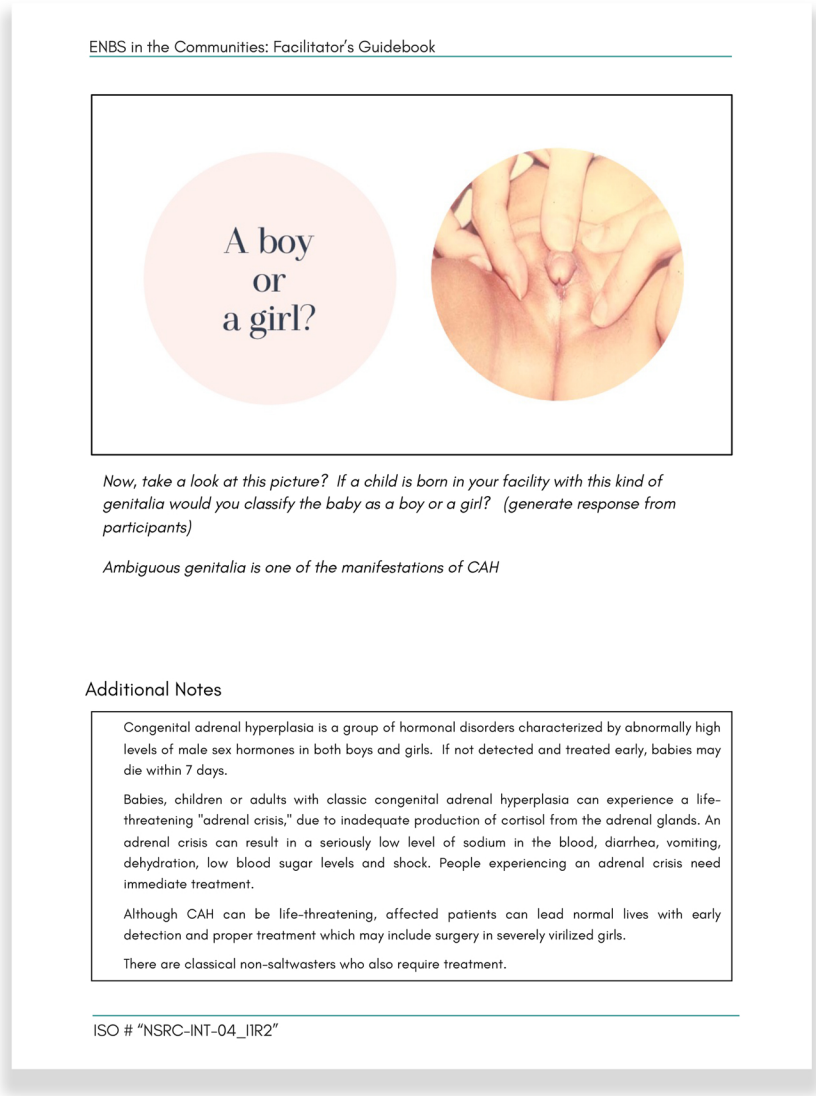
Inserts:	Newborn Screening AVP and Videos
Year of Revision:	2023

HOW TO USE THIS BOOK

THE FORMAT


ENBS in the Communities: Facilitator's Guidebook

A boy or a girl?

Now, take a look at this picture? If a child is born in your facility with this kind of genitalia would you classify the baby as a boy or a girl? (generate response from participants)

Ambiguous genitalia is one of the manifestations of CAH

Additional Notes

Congenital adrenal hyperplasia is a group of hormonal disorders characterized by abnormally high levels of male sex hormones in both boys and girls. If not detected and treated early, babies may die within 7 days.

Babies, children or adults with classic congenital adrenal hyperplasia can experience a life-threatening "adrenal crisis," due to inadequate production of cortisol from the adrenal glands. An adrenal crisis can result in a seriously low level of sodium in the blood, diarrhea, vomiting, dehydration, low blood sugar levels and shock. People experiencing an adrenal crisis need immediate treatment.

Although CAH can be life-threatening, affected patients can lead normal lives with early detection and proper treatment which may include surgery in severely virilized girls.

There are classical non-saltwasters who also require treatment.

ISO # "NSRC-INT-04_I1R2"

Actual slide presentation

Suggested script for the Speaker

Some facts and details/points for discussion and issues that may aid the speaker

The *suggested script* for the speaker is in italics.

Additional notes for the speaker are written at the bottom of the page.

All points to be emphasized are in italic bold format.

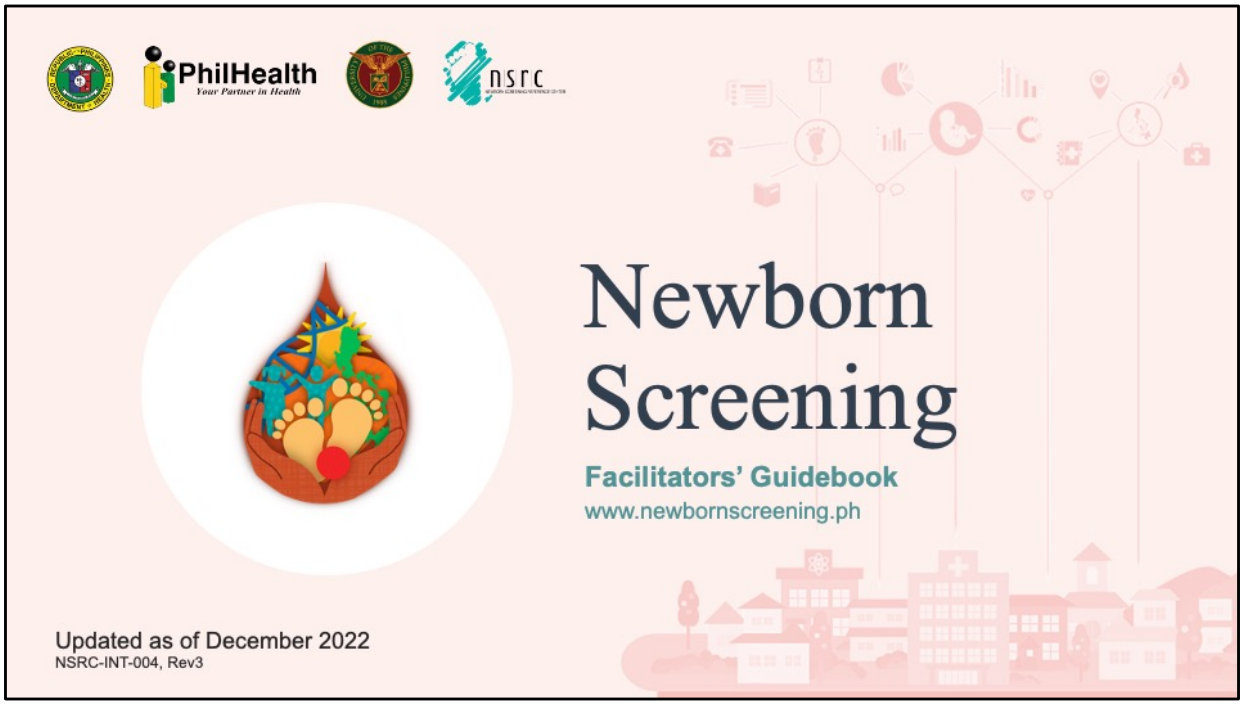
This book comes with an 8-minute AVP to highlight steps for implementing newborn screening at the community level.

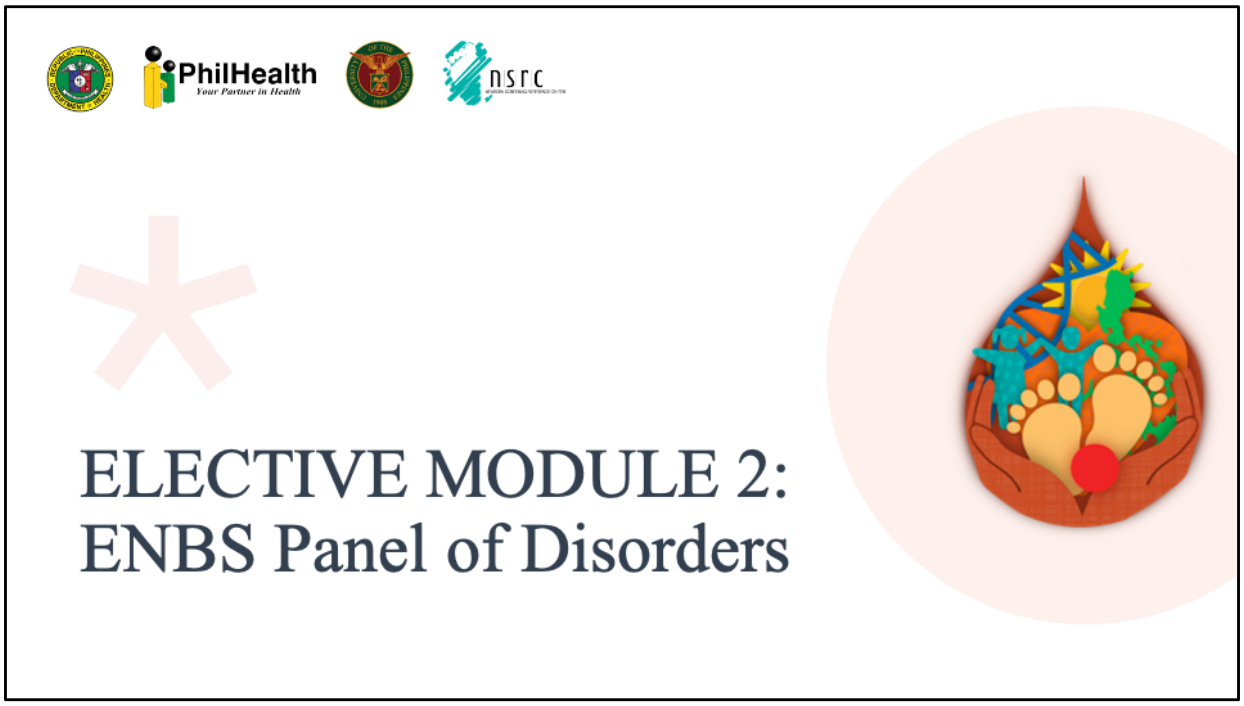
ACRONYMS

3MCC	3-Methylcrotonyl CoA Carboxylase Deficiency
6-PTPS	6-Pyruvoyltetrahydrobiopterin synthase Deficiency
ACNBS	Advisory Committee on Newborn Screening
ASA	Argininosuccinic Aciduria
BKT	Beta Ketothiolase Deficiency
BTD	Biotinidase Deficiency
CAH	Congenital Adrenal Hyperplasia
CF	Cystic Fibrosis
CH	Congenital Hypothyroidism
CIT	Citrullinemia
CPT	Carnitine Palmitoyltransferase Deficiency
CUD	Carnitine Uptake Deficiency
DOH	Department of Health
DOH-RO	Department of Health-Regional Office
ENBS	Expanded Newborn Screening
GAL	Galactosemia
G6PD	Glucose-6-Phosphate Dehydrogenase Deficiency
GA	Glutaric Acidemia
HFSRB	Health Facilities and Services Regulatory Bureau
HGB	Hemoglobinopathies
HCY	Homocystinuria
IRR	Implementing Rules and Regulations
IVA	Isovaleric Acidemia
LCHAD	Long Chain Hydroxyacyl-CoA Dehydrogenase Deficiency

ACRONYMS

LGU	Local Government Unit
MAT	Methionine Adenosine Transferase Deficiency/ Hypermethioninemia
MSUD	Maple Syrup Urine Disease
MCAD	Medium Chain-Acyl-CoA Dehydrogenase Deficiency
MMA	Methylmalonic Acidemia
MCD	Multiple Carboxylase Deficiency
NBS	Newborn Screening
NCP	Newborn Care Package
NIH	National Institutes of Health
NSC	Newborn Screening Center
NSF	Newborn Screening Facility
NSRC	Newborn Screening Reference Center
PA	Propionic Acidemia
PHIC	Philippine Health Insurance Corporation
PKU	Phenylketonuria
RHU	Rural Health Unit
TFP	Tri-functional Protein Deficiency
TYR	Tyrosinemia
VLCAD	Very Long Chain-Acyl-CoA Dehydrogenase Deficiency



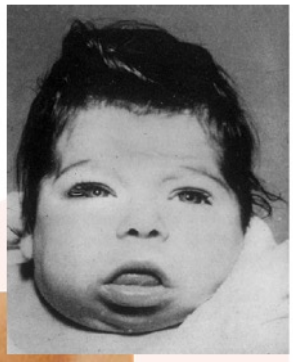


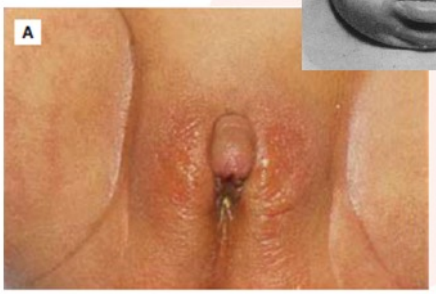
This module is optional for refresher courses

What Disorders are Tested in ENBS?

1. Endocrine Disorders

Babies with endocrine disorders of either the thyroid or andrenal glands make too little of certain hormones. This causes growth and development problems, among other issues.





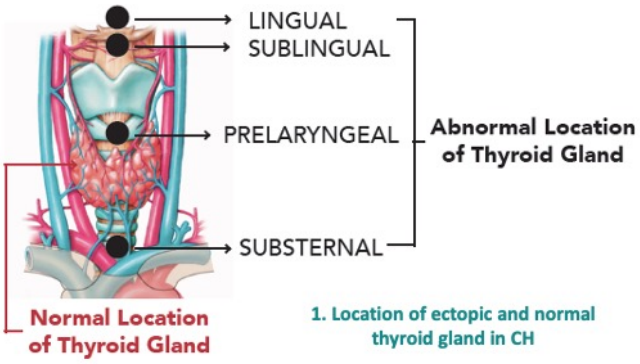
Additional Notes

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.

Meanwhile, 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.

What Disorders are Tested in ENBS?

1. **Endocrine Disorders include:**
   - Congenital Hypothyroidism (CH)
   - Congenital Adrenal Hyperplasia (CAH)



1. Location of ectopic and normal thyroid gland in CH

Newborn Screening Reference Center

There are two disorders under Endocrine Disorders: Congenital Hypothyroidism or CH and Congenital Adrenal Hyperplasia or CAH.

Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation in children. According to the Philippine NBS data, (December 2021) 1 out of 2,649 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.

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-hydroxylase 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 2021 reports that 1 out of 20,589 screened newborns have CAH.

What Disorders are Tested in ENBS?

1. Endocrine Disorders

CH Symptoms:
- Jaundice
- Constipation
- Large fontanelle (soft spot on the head)
- Large tongue

CH Treatment:
- Hormone (Levothyroxine) replacement

CAH Symptoms:
- Dehydration
- Poor feeding
- Diarrhea
- Vomiting
- Ambiguous genitalia
- Low blood glucose
- Low blood sodium levels

CAH Treatment:
- Glucocorticoid and mineralcorticoid replacement therapy

Newborn Screening Reference Center

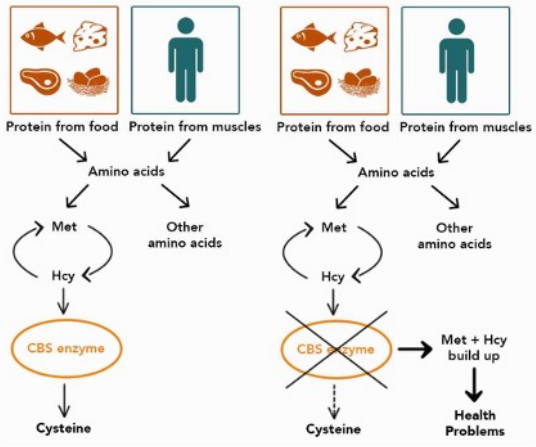
Immediate diagnosis and treatment of congenital hypothyroidism in the neonatal period is critical to normal brain development and physical growth. Treatment started within the first two weeks of life usually prevents neurodevelopmental delays. Recommended treatment is the lifetime daily administration 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.

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.

What Disorders are Tested in ENBS?

2. Amino Acid Disorders

Occur when the body cannot either metabolize or produce certain amino acids which results in toxic accumulation of substances



Normal breakdown of protein vs.
Homocystinuria patient's breakdown of protein

Amino acid disorders are conditions that occur when a person's body cannot break down certain types of amino acids. Amino acids are the building blocks of protein. Normally, when we eat, our bodies digest or break down food into protein. Protein is then broken down into amino acids. Our bodies use amino acids to make energy. Enzymes (special proteins that help our bodies perform chemical reactions) usually help our bodies break down food and make energy.

A person with an amino acid disorder is either missing at least one enzyme, or their enzymes do not work correctly. When these enzymes are missing or do not work, food cannot be broken down and made into energy. If food cannot be broken down, dangerous substances build up in the body. This build-up can happen shortly after birth.

What Disorders are Tested in ENBS?

2. Amino Acid Disorders include:

- Homocystinuria (HCY)
- Hypermethioninemia/Methionine Adenosine Transferase Deficiency (MAT)
- Maple Syrup Urine Disease (MSUD)
- Phenylketonuria (PKU), Hyperphenylalaninemia, 6-PTPS Deficiency
- Tyrosinemia Types I, II, III (TYR)

There are five disorders under Amino Acid Disorders: Homocystinuria (HCY), Hypermethioninemia/Methionine Adenosine Transferase Deficiency (MAT), Maple Syrup Urine Disease (MSUD), Phenylketonuria (PKU), Tyrosinemia Types I, II, III (TYR)

What Disorders are Tested in ENBS?

2. Amino Acid Disorders

Symptoms:

- Seizures, coma, developmental delay, death

Treatment:

- Limit protein, provide special medical formula, co-factors or supplements, decrease substrate

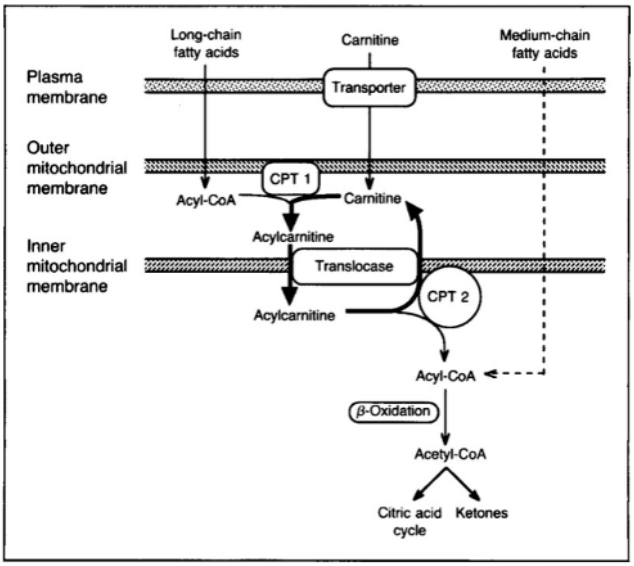
There is no cure for amino acid disorders. However, there are special diets and supplements that can help with the symptoms. Children who have amino acid disorders will need to be on these treatments for the rest of their lives.

Good medical care makes a difference for children with amino acid disorders. These children should see a metabolic geneticist (a doctor who specializes in amino acid disorders and other related conditions) as well as their pediatrician. Together, they will set up treatment, tests, or appointments according to the child's needs.

What Disorders are Tested in ENBS?

3. Fatty Acid Oxidation Disorders

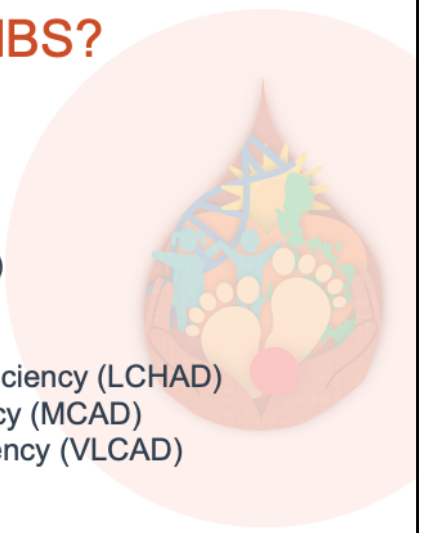
Breakdown of fatty acids in mitochondria is an essential part of body's ability to produce energy. Fatty Acid Oxidation Disorders is described by the body's inability to break down fatty acids.



Newborn Screening Reference Center

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.

What Disorders are Tested in ENBS?



3. Fatty Acid Oxidation Disorders include:

- Carnitine Palmitoyltransferase I Deficiency (CPT1)
- Carnitine Palmitoyltransferase II Deficiency (CPT2)
- Carnitine Uptake Deficiency (CUD)
- Glutaric Acidemia Type II (GA II)
- Long Chain Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)
- Medium Chain-Acyl-CoA Dehydrogenase Deficiency (MCAD)
- Very Long Chain-Acyl-CoA Dehydrogenase Deficiency (VLCAD)
- Tri-functional Protein Deficiency (TFP)

There are eight disorders under Fatty Acid Oxidation Disorders: Carnitine Palmitoyltransferase I Deficiency (CPT1), Carnitine Palmitoyltransferase II Deficiency (CPT2), Carnitine Uptake Deficiency (CUD), Glutaric Acidemia Type II (GA II), Long Chain Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD), Medium Chain-Acyl-CoA Dehydrogenase Deficiency (MCAD), Very Long Chain-Acyl-CoA Dehydrogenase Deficiency (VLCAD), Tri-functional Protein Deficiency (TFP)

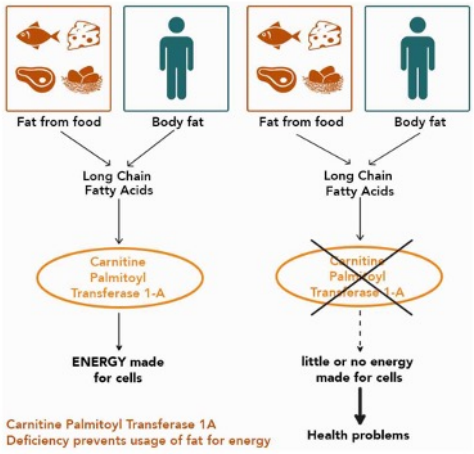
What Disorders are Tested in ENBS?

3. Fatty Acid Oxidation Disorders

Symptoms:

- Decompensate with any metabolic stress -fever, fasting, intercurrent illness
- Hypoketotic hypoglycemia, liver, muscle, heart disease
- Lethargy, seizures, coma, sudden death

Treatment: Treatment is through the dietary restriction of fat, and avoidance of fasting. Carnitine supplementation is needed for CUD. VLCAD patients are treated with a special milk formula containing medium chain triglycerides.



Normal breakdown of protein vs.
CPT1 patient's breakdown of protein

Newborn Screening Reference Center

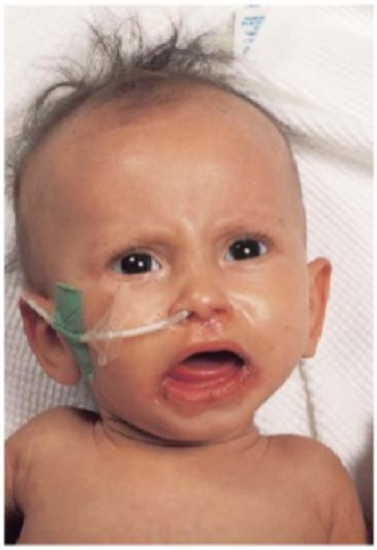
Additional Notes

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 Disorders are Tested in ENBS?

4. Organic Acid Disorders

- The body cannot metabolize certain acids and fats
- Accumulation of organic acids in blood and urine
- Serious potentially preventable effects on health and development, including death.



Nyhan et al. Atlas of Metabolic Diseases. 2005.

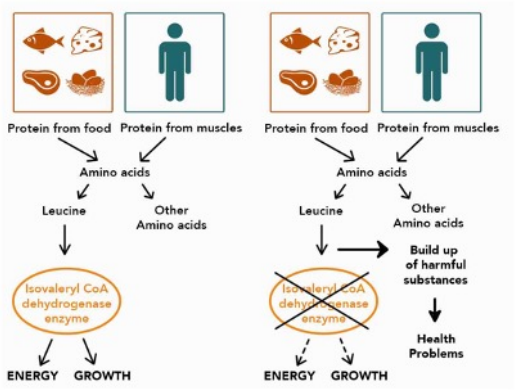
Figure 3.4 *This infant with methylmalonic acidemia had also failed to thrive and was anorexic. She also had alopecia.*

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.

What Disorders are Tested in ENBS?

4. Organic Acid Disorders include:

- 3-methylcrotonyl-CoA carboxylase deficiency
- Beta Ketothiolase Deficiency (BKD)
- Glutaric Acidemia Type I (GA I)
- Isovaleric Acidemia (IVA)
- Methylmalonic Acidemia (MMA)
- Multiple Carboxylase Deficiency (MCD)
- Propionic Acidemia (PA)

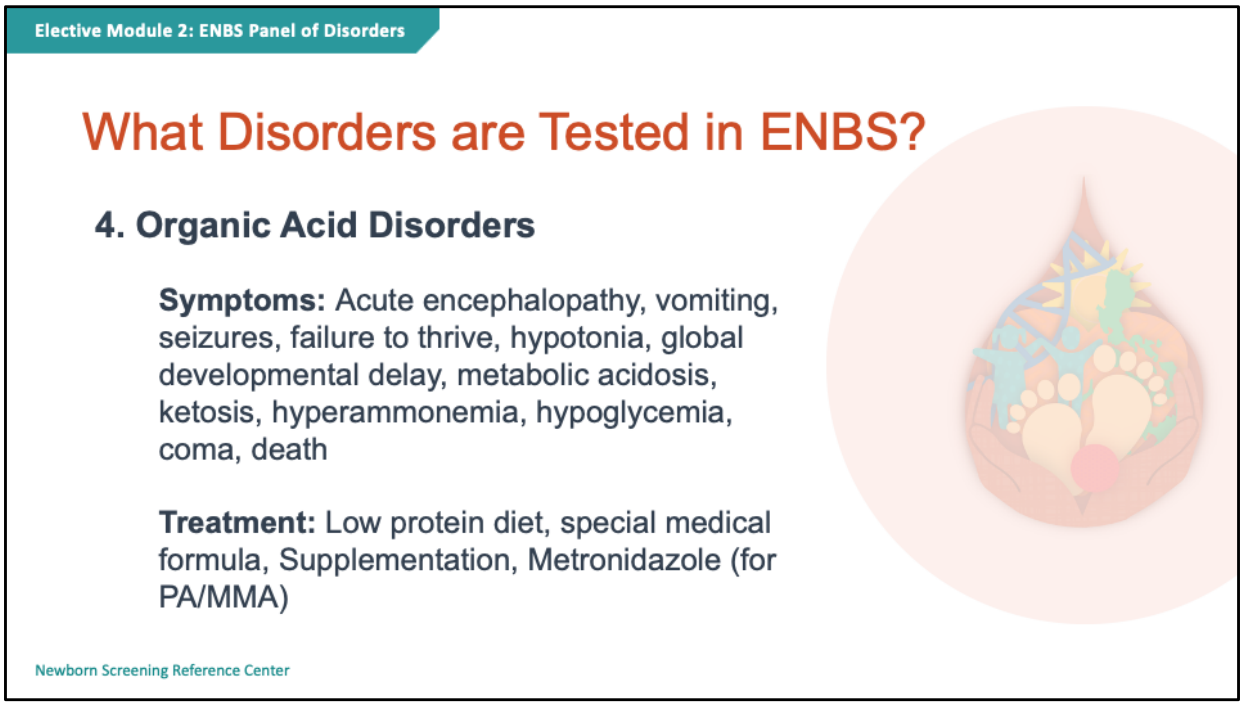


Normal breakdown of protein vs.
BKD patient's breakdown of protein

Newborn Screening Reference Center

The disorders their names from the substance that accumulates proximal to the block in the pathway. They are the following:

- *3-methylcrotonyl-CoA carboxylase deficiency*
- *Beta Ketothiolase Deficiency*
- *Glutaric Aciduria Type 1*
- *Isovaleric aciduria (IVA) – due to a deficiency of isovaleryl-CoA dehydrogenase*
- *Methylmalonic aciduria (MMA) – due to a deficiency of methymalonyl-CoA mutase*
- *Multiple Carboxylase Deficiency (MCD)*
- *Propionic aciduria (PA) – due to a deficiency of propionyl-CoA carboxylase*



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.

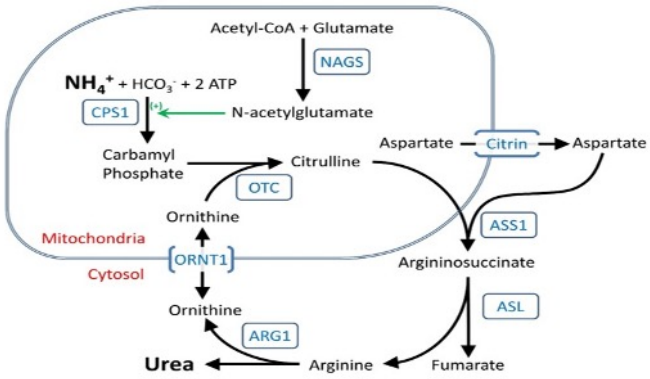
Treatment is through the dietary restriction of protein. Children may be given a special medical formula that is protein free. Carnitine and/or glycine are also prescribed.

Elective Module 2: ENBS Panel of Disorders

What Disorders are Tested in ENBS?

5. Urea Cycle Defects

- The urea cycle is responsible for detoxification of ammonia to urea
- Urea cycle defects result from inherited defects in any of the steps if the pathway, except for OTCD*



*Ornithine transcarbamylase defucuency –X-linked recessive

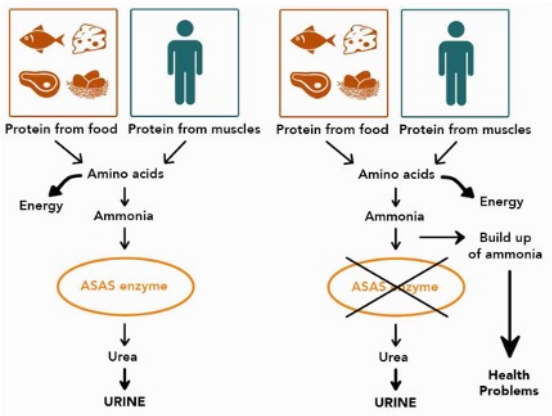
Urea Cycle Disorders Overview. *GeneReviews*. Retrieved from: https://www.ncbi.nlm.nih.gov/books/NBK1217/figure/ucd-overview.F1/?report=objectonly

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. 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.

What Disorders are Tested in ENBS?

5. Urea Cycle Defects include:

- Citrullinemia type 1
- Argininosuccinic Aciduria (ASA)



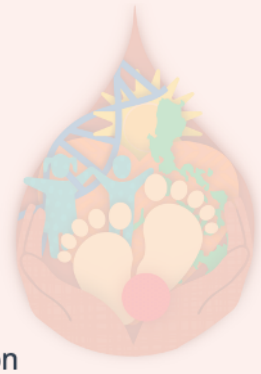
Normal breakdown of protein vs.
CIT patient's breakdown of protein

Newborn Screening Reference Center

There are two disorders under Urea Cycle Defects: Citrullinemia type 1 and Argininosuccinic Aciduria, both are inherited in an autosomal recessive manner. Citrullinemia type 1 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.

What Disorders are Tested in ENBS?

5. Urea Cycle Defects



Symptoms: Acute encephalopathy, vomiting, seizures, failure to thrive, hypotonia, global developmental delay, metabolic acidosis, ketosis, hyperammonemia, hypoglycemia, coma, death

Treatment: Low protein diet, special medical formula
For ASA and Citrullinemia type 1, arginine supplementation

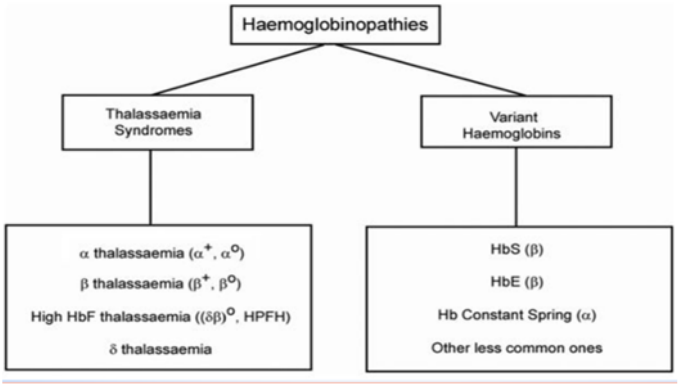
Additional Notes

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.

What Disorders are Tested in ENBS?

6. Hemoglobinopathies (HGB)

- Hemoglobinopathies arise from defective genes coding for abnormal hemoglobins



Newborn Screening Reference Center

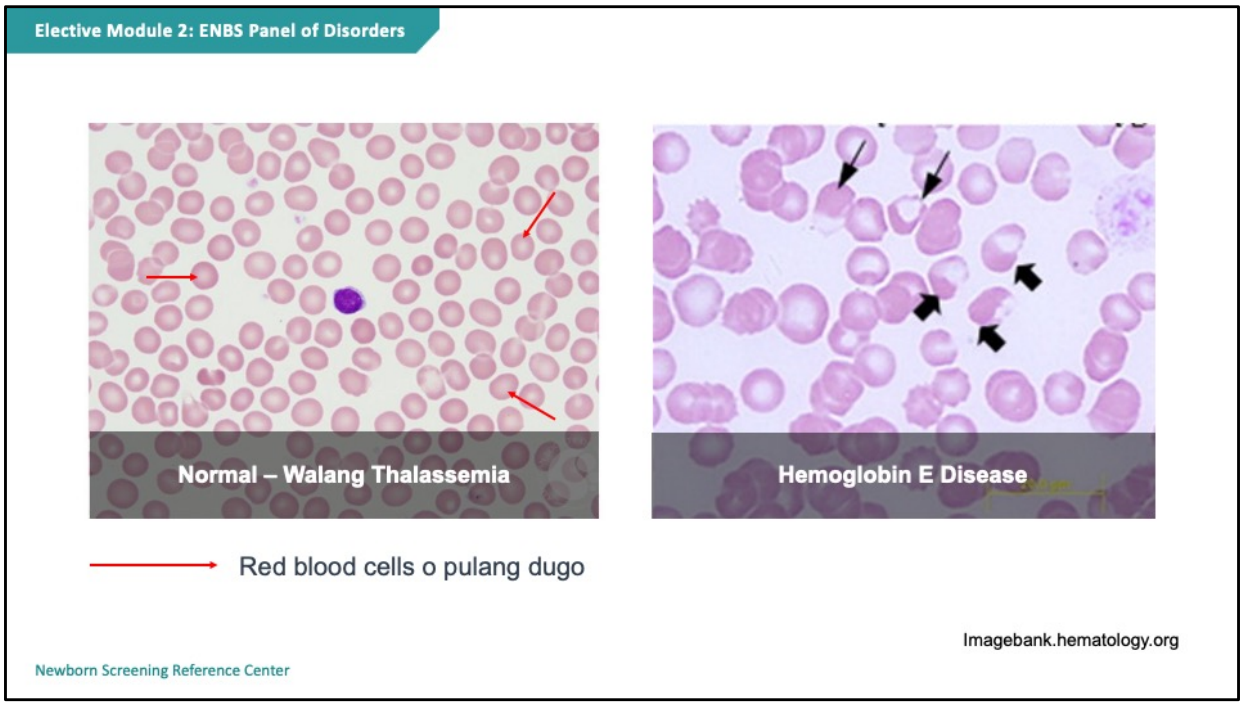
Hemoglobinopathies are structural abnormalities and are usually due to a single amino acid substitution. These disorders exhibit unique geographical distribution. HbS, HbSC, HbS/β thalassemia or sickle cell disease is typically common in Africa, Saudi Arabia, India and in the Americas. HbE is almost exclusively from South East Asia.

What Disorders are Tested in ENBS?

6. Hemoglobinopathies (HGB) include:

- Alpha Thalassemia
- Beta Thalassemia
- Hemoglobin C
- Hemoglobin D
- Hemoglobin E
- Sickle Cell Disease

There are six disorders under Hemoglobinopathies: Alpha Thalassemia, Beta Thalassemia, Hemoglobin C, Hemoglobin D, Hemoglobin E, and Sickle Cell Disease



This is what our blood looks like under the microscope.

The first is a photo of red blood cells with normal hemoglobin. They are round in shape, and has a bit of white in the middle. These cells are identical in shape and size.

However, you can observe in the second picture that there are less number of red blood cells and they differ in shape.

Why do the red blood cells look like that? That's because there's something wrong with how the instructions are given to make the hemoglobin, which happens as a result of a gene mutation.

If a child has a Hemoglobin E disease, their red blood cells are easily destroyed which can lead to anemia.

What Disorders are Tested in ENBS?

6. Hemoglobinopathies (HGB)

Symptoms:
- Weakness and fatigue due to anaemia
- Shortness of breath

Treatment: Treatment options and recommendations differ between types of hemoglobinopathies

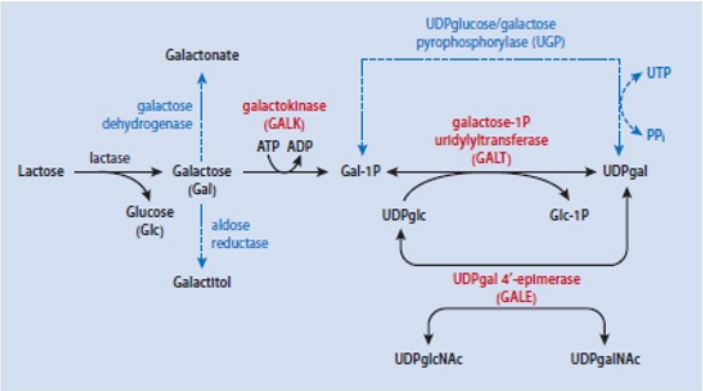
Thalassemias are characterized by a decreased production in the either the α or β globin chains. They are grouped into α and β thalassemias. The imbalance in the production of globin chain results in a haemolytic anemia or precipitation of the red cells in the bone marrow or a process known as ineffective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

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

What Disorders are Tested in ENBS?

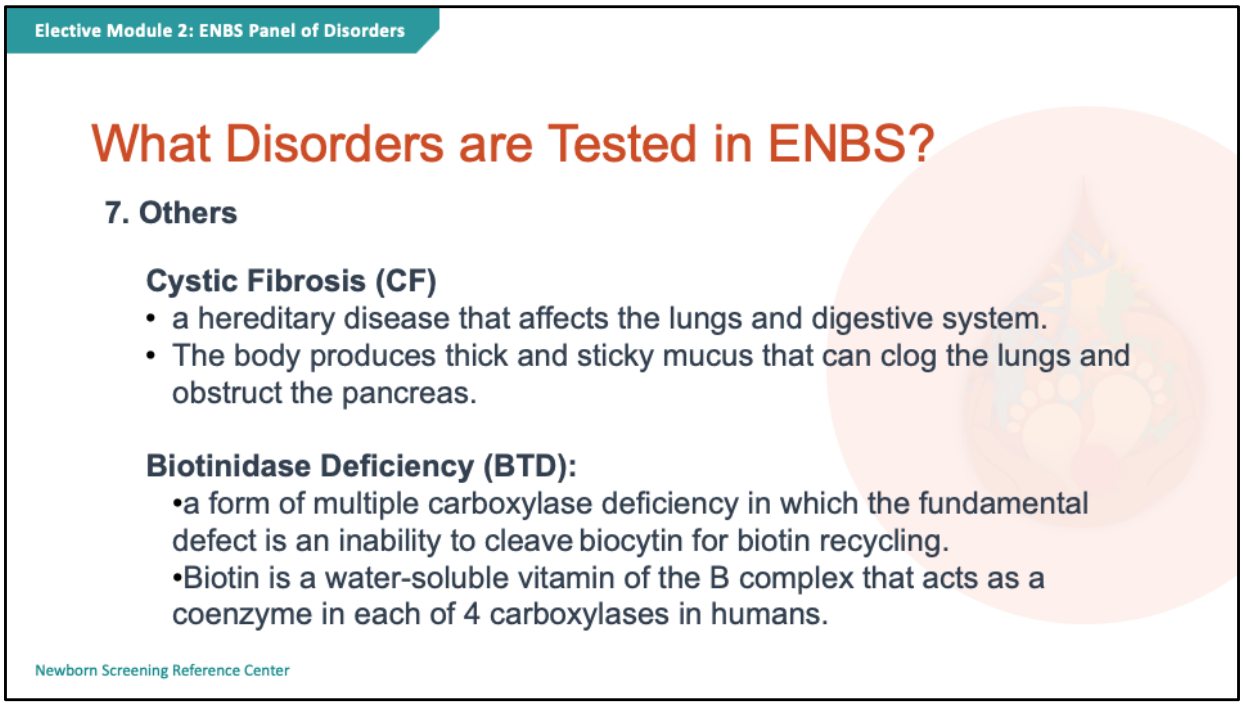
7. Others

- Galactosemia (GAL)
- Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency
- Cystic Fibrosis (CF)
- Biotinidase Deficiency (BTD)



Newborn Screening Reference Center

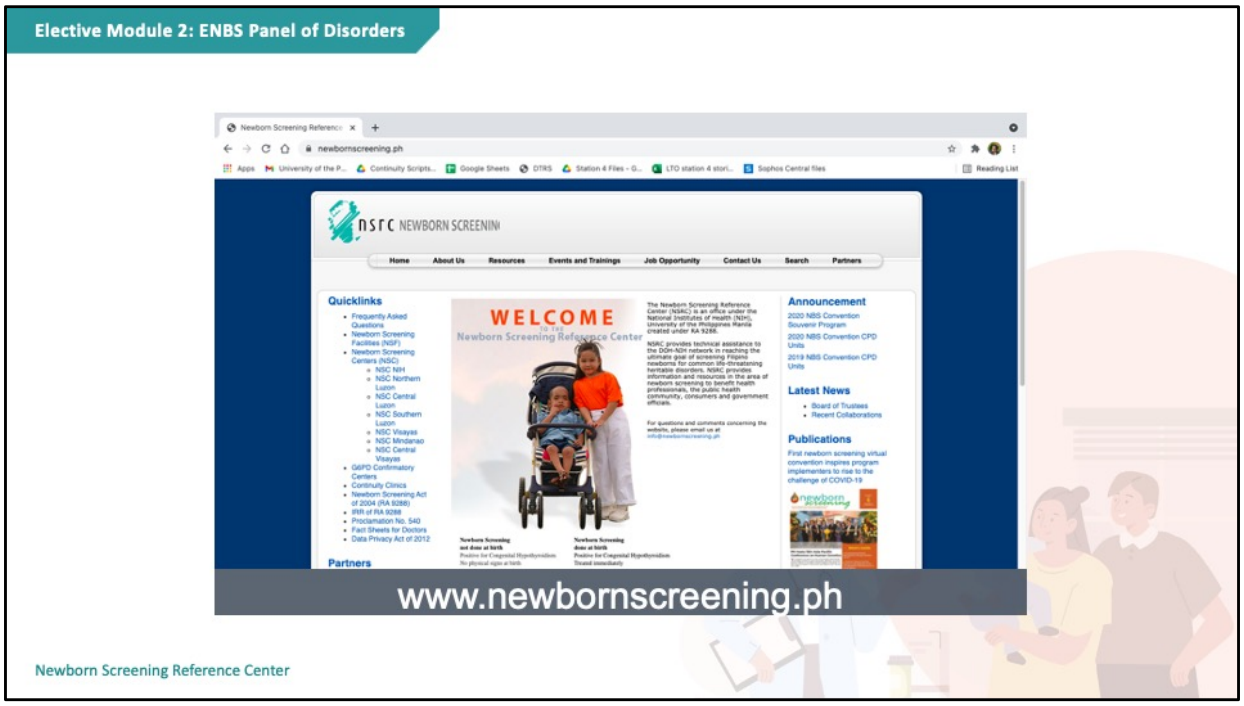
There are four other disorders that are tested in the expanded newborn screening panel, these are: Galactosemia (GAL), Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency, Cystic Fibrosis (CF), and Biotinidase Deficiency (BTD)



Additional Notes

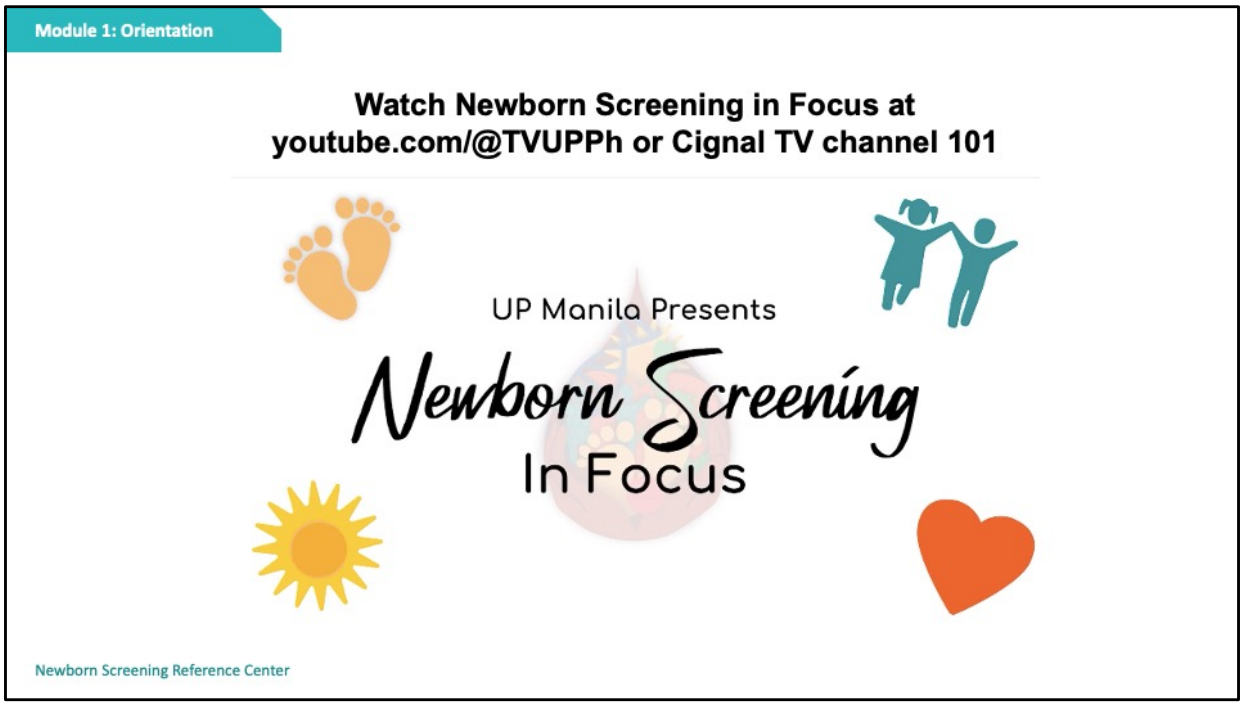
In people with Cystic FIbrosis, mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene cause the CFTR protein to become dysfunctional. When the protein is not working correctly, it's unable to help move chloride -- a component of salt -- to the cell surface. Without the chloride to attract water to the cell surface, the mucus in various organs becomes thick and sticky. In the lungs, the mucus clogs the airways and traps germs, like bacteria, leading to infections, inflammation, respiratory failure, and other complications. For this reason, avoiding germs is a top concern for people with CF.

Biotinidase deficiency presents with a median age of 3 months or as late as 10 years of age, symptoms include dermatologic affectation appearing as patchy desquamation and neurological manifestations such as seizures in 70% of patients and ataxia that can interfere with walking. Some patients may also have op c atrophy and hearing loss Individuals with partial biotinidase deficiency can present with skin manifestations and no neurologic symptoms.



For more information about newborn screening, you can visit the newborn screening resource/portal site:

www.newbornscreening.ph



Newborn Screening in Focus is a video series that uncovers the wonderful story of Newborn Screening in the Philippines, zooming in on what makes Newborn Screening a comprehensive program for every Filipino.

NBS in Focus features the humble beginnings of the Newborn Screening Program and its evolution into a national health program. The series also presents the very process of newborn screening from the moment the child is born, and into the continuing care available for newborns confirmed to have a disorder included in the panel. Features and management of the disorders from the newborn screening panel are also discussed in individual episodes. Finally, the series presents the Newborn Screening program network, and how the program managed to give quality service despite the limits brought about by disasters such as the COVID-19 pandemic.

Watch the live airing of NBS in Focus every Saturday 7-8 pm at Cignal TV 101 or online at youtube.com/@TVUPPh.