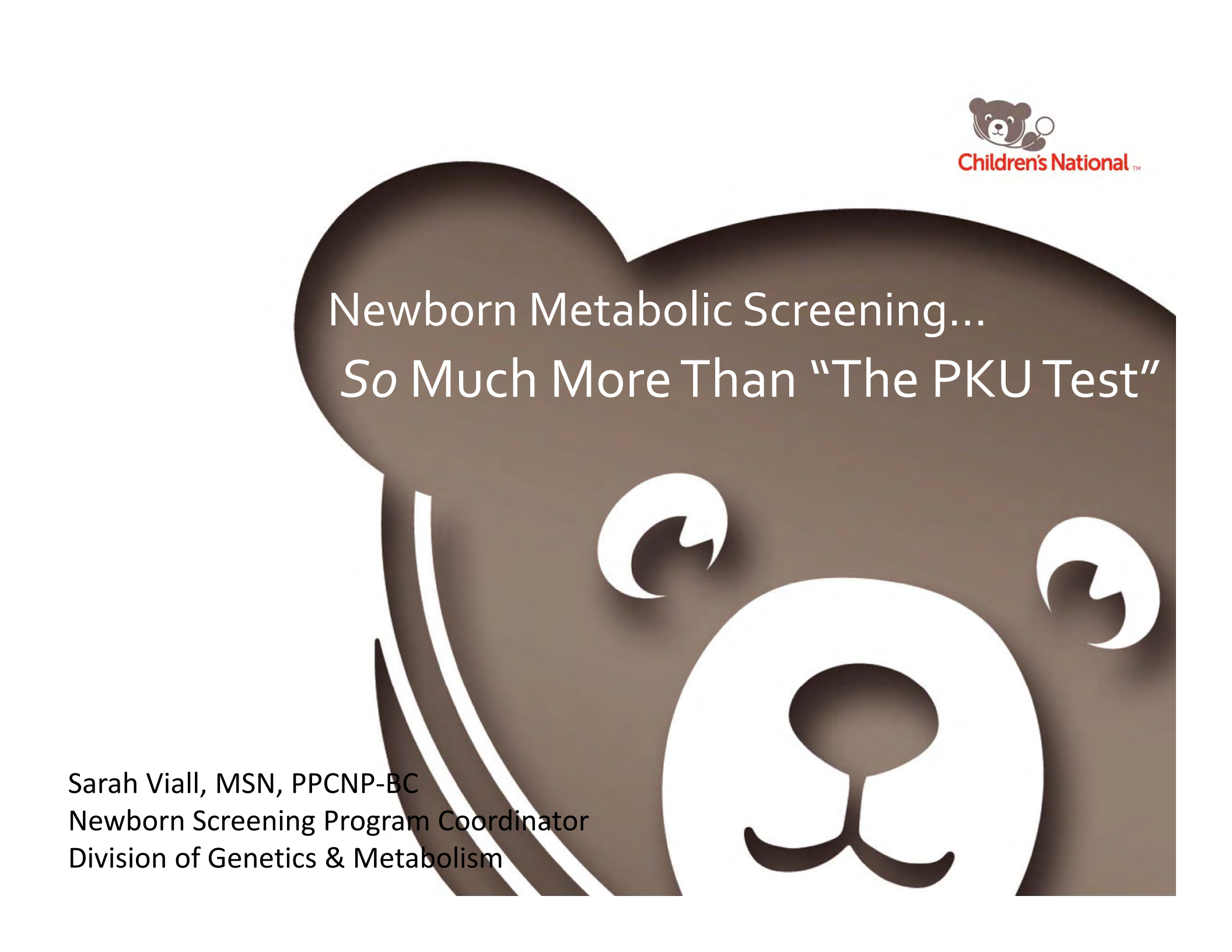

Sarah Viall, MSN, PPCNP-BC
Newborn Screening Program Coordinator
Division of Genetics & Metabolism

Conflicts of Interest

I have no conflicts of interest to disclose.

Children's National™

Case 1: Katy

7 day old for one week well-child check

PMHx

- 38 weeks GA, NSVD, Apgars 8 and 9, BW 2.98 kg
- Discharged home DOL 4 with no complications, breast feeding

Before you walk into the room…

- Weight 2.94 kg
- Breastfeeding "well", completes ~ 20 minute feed
- Waking to feed, parents describe as "alert, healthy"

Case 1

NEWBORN SCREENING PROGRAM
VIRGINIA DEPARTMENT OF GENERAL SERVICES
DIVISION OF CONSOLIDATED LABORATORY SERVICES
600 North 5th Street, Richmond VA 23219
(804) 648-4480
Toll Free (866) 378-7730

Report Date : 01/28/2015

Print Date : 01/28/2015
Print Time : 12:29 pm

Baby's Name/Mother's Name

Sample #: Device ID: First Lab#:

Birth Date: /2015 Collection Date: 01/ /2015
Birth Time: 0951 Collection Time: 1740
Receive Date: 2015

MedicalID: Folder#:

SEND TO: S-10574
INOVA FAIRFAX HOSPITAL
LABORATORY SERVICES BSMT
3300 GALLOWS RD
FALLS CHURCH VA 22046

Physician: INOVA CARES CLINIC
Hosp. of Birth: INOVA ALEXANDRIA HOSPITAL

Mother's Address:

Tests performed	Normal Results	Result	Normal range
Biotinidase Screen	Within Normal Limits		
CAH	Within Normal Limits		
FATTY ACID OXIDATION PROFI	Within normal limits		
Galactose Screen - Beutler Screen	Within Normal Limits		
Hemoglobinopathy Screen	Normal Newborn Hemoglobin		
IRT- Cystic Fibrosis	Within Normal Limts		
ORGANIC ACIDEMIA PROFILE	Within normal limits		
T4 PROFILE	Within normal limits		
Neonatal TSH Screen	Within Normal Limits		

Tests performed	Abnormal Results	Result		Normal range
ABNORMAL AMINO ACID PROFILE				
Maple Syrup Urine Disease Screen	Above Normal Limits	313.03	umol/L	< 222.000 umol/L

SEND REPEAT BLOOD SPOT TO CONSOLIDATED LABORATORY SERVICE IMMEDIATELY

* See attached document for all tests performed

Case 1: Katy

Tests performed	Abnormal Results	Result	Normal range
ABNORMAL AMINO ACID PROFILE			
Maple Syrup Urine Disease Screen	Above Normal Limits	313.03 umol/L	< 222.000 umol/L

SEND REPEAT BLOOD SPOT TO CONSOLIDATED LABORATORY SERVICE IMMEDIATELY

What Next?

ATTENTION HEALTH CARE PROVIDER:

At the time of routine newborn screening, this baby was screened for genetic or metabolic disorders as required by the State of Virginia. A laboratory report is enclosed for your records. The results of this screening indicate:

Maple Syrup Urine Disease Screen	Above Normal Limits	313.03 umol/L

It is necessary that our laboratory confirm these findings by performing additional testing on a repeat filter paper blood spot collected by a heelstick from the infant. Please submit this sample to us AS SOON AS POSSIBLE with all pertinent requested information. The results will be forwarded to you as soon as they are available.

Clinical information concerning these results is available through the Virginia Newborn Screening Services of the Virginia Department of Health at (804) 864-7714 or (804) 864-7715. Laboratory information can be obtained by calling the Newborn Screening Laboratory at (804) 648-4480 or Toll free at (866) 378-7730 at the Department of General Services, Division of Consolidated Laboratories.

Case 1: Katy

PE: "mild odor of pancakes/maple syrup"

PNP calls Metabolic Specialist

Immediate visit

- Plasma amino acids:
  - Leucine = 2,100 umol/L (48-160) 
  - Isoleucine = 560 umol/L (26-91)
  - Valine = 820 umol/L (44-190)
  - Alloisoleucine = 165 umol/L (0-5)

Diagnosis: Maple Syrup Urine Disease (MSUD)

Newborn Screen Basics

Children's National

Terminology

- Newborn Screen (NBS)
- Newborn Metabolic Screen (NMS)
- Expanded Newborn Screen

<u>**NOT**</u> the "PKU Test"

Children's National

Take Home Points

NOT the "PKU Test"

Anxiety reduction

Use resources and support!

Children's National

Communication of Results

Every state follow-up program is different

Contact order varies

When contacting families…

- Recognized provider
- Abnormal ≠ positive
  - Screening NOT diagnostic test
- Treatable disorders

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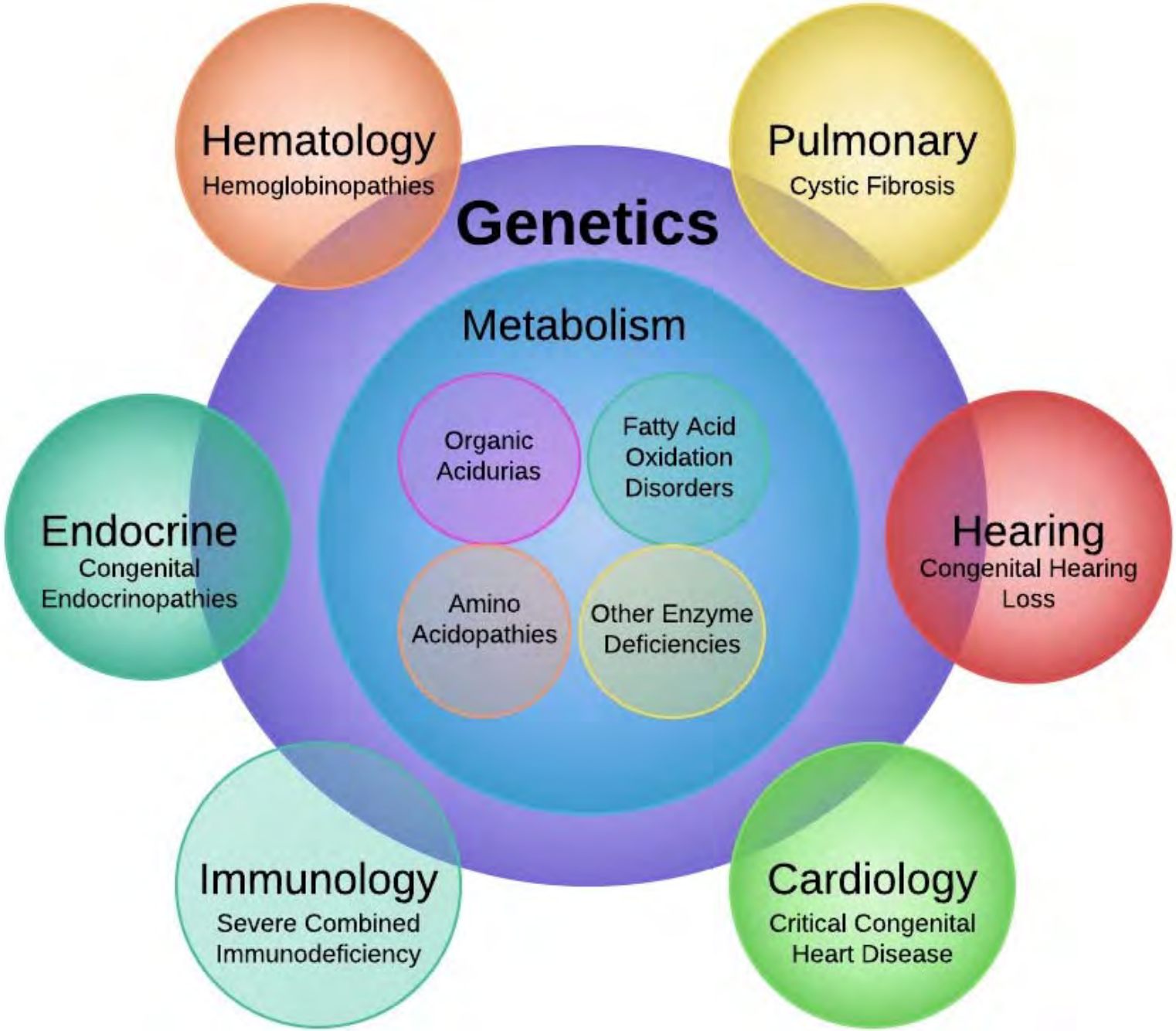
Metabolic Disorders of the Newborn Screen

Children's National™


Hematology
Hemoglobinopathies
Pulmonary
Cystic Fibrosis
Genetics
Metabolism
Organic Acidurias
Fatty Acid Oxidation Disorders
Amino Acidopathies
Other Enzyme Deficiencies
Endocrine
Congenital Endocrinopathies
Hearing
Congenital Hearing Loss
Immunology
Severe Combined Immunodeficiency
Cardiology
Critical Congenital Heart Disease

Recommended Uniform Screening Panel (RUSP)

ACMG Code	Core Condition	Metabolic Disorder					Other Disorder
		Organic acid condition	Fatty acid oxidation disorders	Amino acid disorders			
PROP	Propionic acidemia	X					
MUT	Methylmalonic acidemia (methylmalonyl-CoA mutase)	X					
Cbl A,B	Methylmalonic acidemia (cobalamin disorders)	X					
IVA	Isovaleric acidemia	X					
3-MCC	3-Methylcrotonyl-CoA carboxylase deficiency	X					
HMG	3-Hydroxy-3-methyglutaric aciduria	X					
MCD	Holocarboxylase synthase deficiency	X					
ßKT	ß-Ketothiolase deficiency	X					
GA1	Glutaric acidemia type I	X					
CUD	Carnitine uptake defect/carnitine transport defect		X				
MCAD	Medium-chain acyl-CoA dehydrogenase deficiency		X				
VLCAD	Very long-chain acyl-CoA dehydrogenase deficiency		X				
LCHAD	Long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency		X				
TFP	Trifunctional protein deficiency		X				
ASA	Argininosuccinic aciduria			X			
CIT	Citrullinemia, type I			X			
MSUD	Maple syrup urine disease			X			
HCY	Homocystinuria			X			
PKU	Classic phenylketonuria			X			
TYR I	Tyrosinemia, type I			X			
CH	Primary congenital hypothyroidism				X		
CAH	Congenital adrenal hyperplasia				X		
Hb SS	S,S disease (Sickle cell anemia)					X	
Hb S/ßTh	S, βeta-thalassemia					X	
Hb S/C	S,C disease					X	
BIOT	Biotinidase deficiency						X
CCHD	Critical congenital heart disease						X
CF	Cystic fibrosis						X
GALT	Classic galactosemia						X
HEAR	Hearing loss						X
SCID	Severe combined immunodeficiences						X

Organic Acid Conditions

Fatty Acid Oxidation Disorders

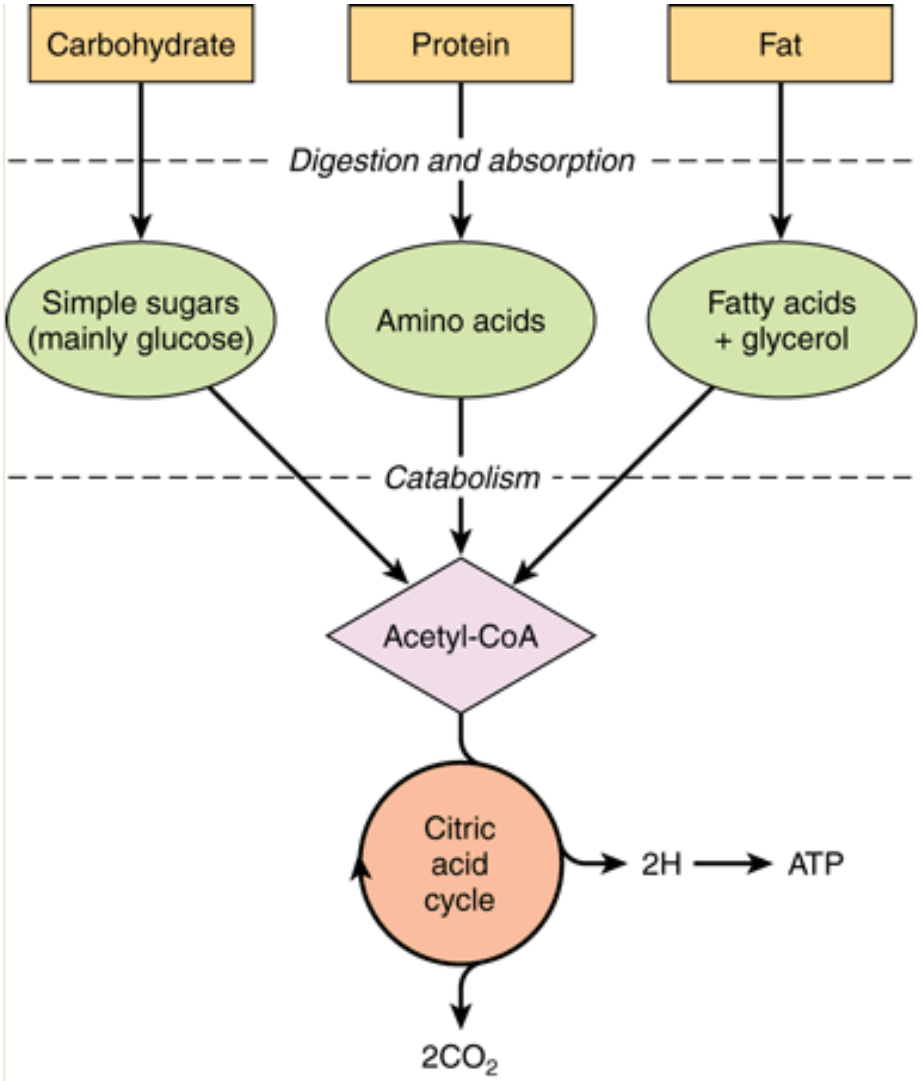
Amino Acid Disorders

Other Metabolic Disorders

Source: http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendedpanel/uniformscreeningpanel.pdf

Children's National

General Principles: Metabolism



Source: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA: *Harper's Illustrated Biochemistry, 29th Edition*: www.accessmedicine.com

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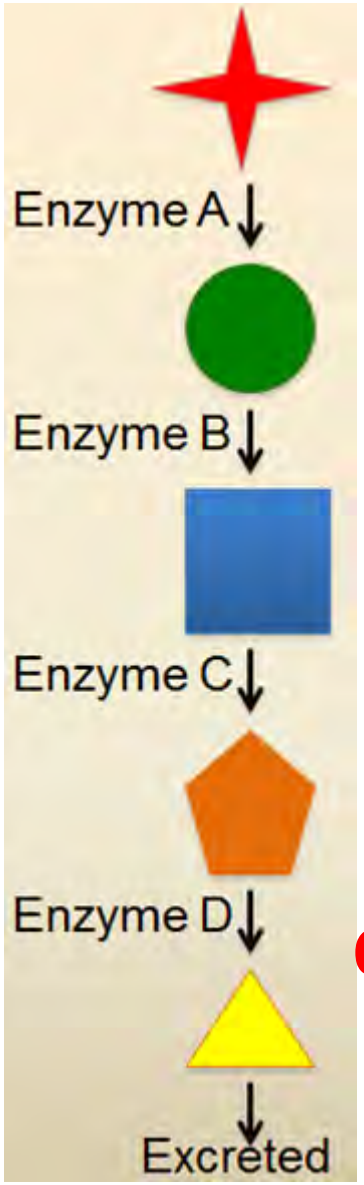
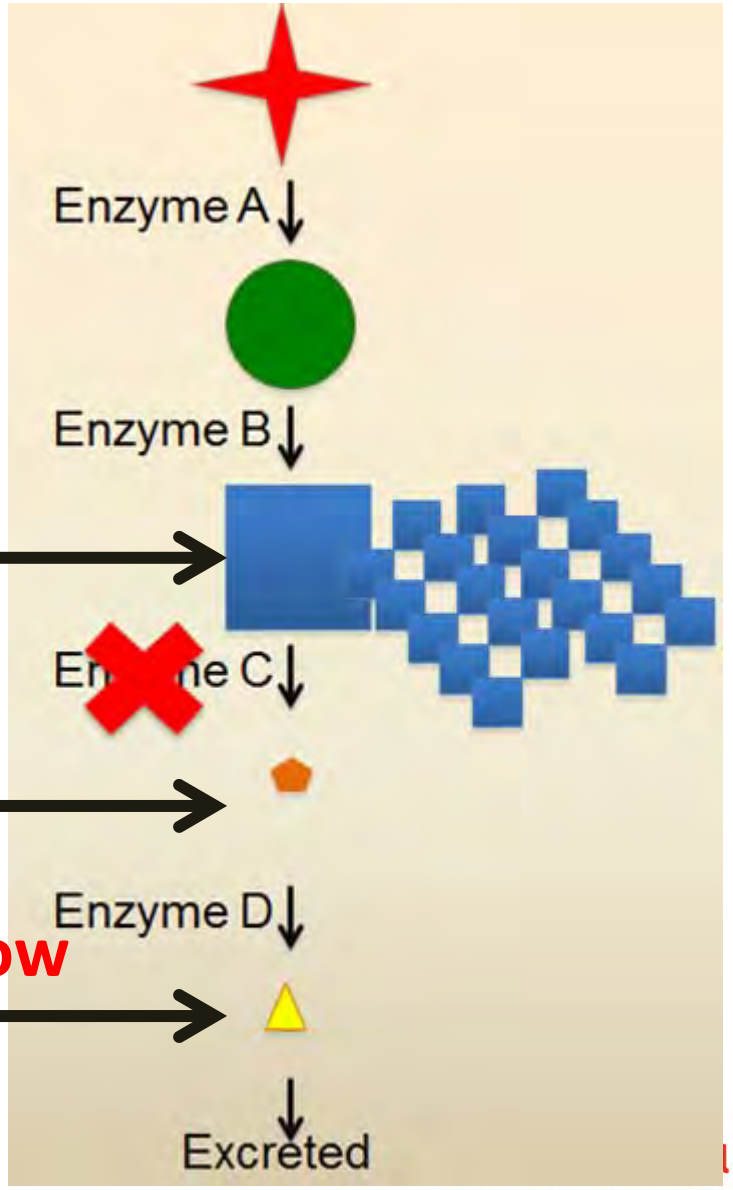
General Principles: Pathophysiology

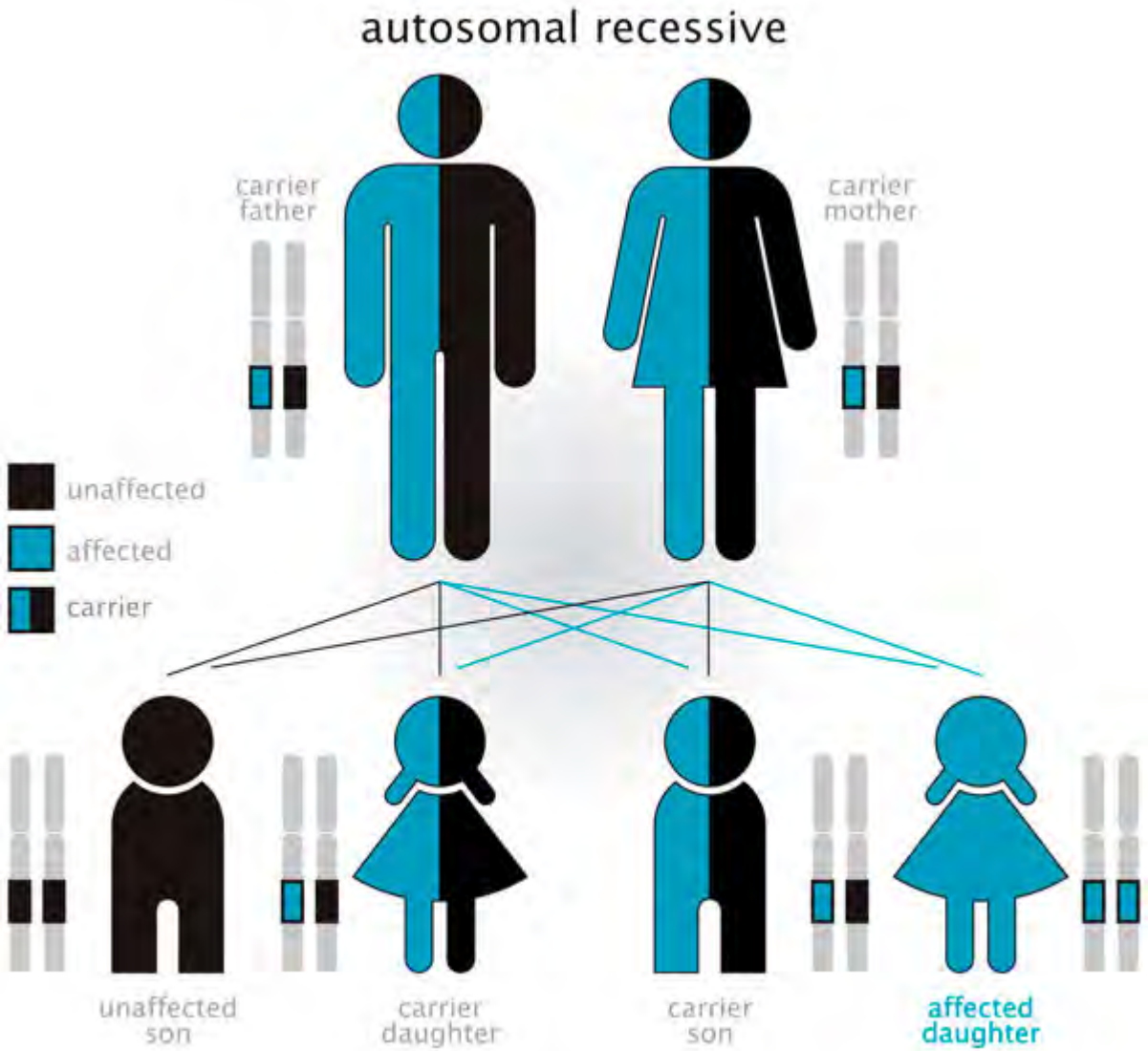
Normal:



Disease:



General Principles: Inheritance



Source: http://www.brusselsgenetics.be/media/images/Illustraties/ill_eng/ill-12-E2_orig.jpg

General Principles: Onset

- Neonatal
  - Poor feeding
  - Vomiting
  - Abnormal tone
  - Odor*
  - Lethargy
  - Seizures
  - Irritability
  - Hyperammonemia
  - Can *quickly* progress to coma or death
- Childhood
- Adulthood

General Principles: Management

Diet changes

Avoidance of fasting

Careful intercurrent illness management

Vitamin supplementation

Medications (rarely)

Abnormal Metabolic Newborn Screen Cases

Children's National™

Case 2: Logan

State of Maryland
Department of Health and Mental Hygiene
Laboratories Administration
201 West Preston Street
Baltimore, Maryland 21201
Lawrence J. Hogan, Jr., Governor - Van T. Mitchell, Secretary
Robert Myers, Ph.D., Director

Maryland Newborn Screening Follow-Up Program
Telephone Number: (410) 767 - 6736
FAX Number: (410) 333 - 5018

CAPITOL MEDICAL GROUP — **Genetic Evaluation:** Childrens National Medical Center

FOR SPECIMEN COLLECTED 03/ /2015 SHOWING GALACTOSE WNL AND REDUCED GALT. THIS REPEAT SPECIMEN WAS
OXIMATELY 40 DAYS OF AGE FROM INFANT TWIN BORN AT 36 WEEKS GESTATION. INFANT USING LACTOSE FORMULA FOR
IOWING GOOD WEIGHT GAIN.
CARRIER FOR CLASSICAL GALACTOSEMIA OR HAS A MILD VARIANT WILL CONTACT PCP TO RECOMMEND QUANTITATIVE GALT
KE THAT DETERMINATION.

Mother: **Certified Letter Date:**

03/ /2015	LLAMMEREE	SPOKE WITH PCP OFFICE ASKING IF REPEAT NBS HAS BEEN COLLECTED. NURSE WILL NEED TO CALL BE BACK.
03/ /2015	LLAMMEREE	RECEIVED CALL BACK FROM NURSE CARRIE AT PCP OFFICE. SHE REPORTED INFANT IS DOING WELL AND REPEAT NBS WAS COLLECTED 03/17/2015 AND MAILED. WILL WATCH FOR REPEAT SPECIMEN.
03/ /2015	WATSONJ	REPEAT SPECIMEN COLLECTED ON 03/13/2015 IS CURRENTLY PENDING.
03/ /2015	LLAMMEREE	RECEIVED REPORT FOR SPECIMEN COLLECTED 03/ /2015 SHOWING GALACTOSE WNL AND REDUCED GALT. THIS REPEAT SPECIMEN WAS OBTAINED AT APPROXIMATELY 40 DAYS OF AGE FROM INFANT TWIN BORN AT 36 WEEKS GESTATION. INFANT USING LACTOSE FORMULA FOR FEEDINGS AND IS SHOWING GOOD WEIGHT GAIN. LIKELY INFANT IS A CARRIER FOR CLASSICAL GALACTOSEMIA OR HAS A MILD VARIANT. WILL CONTACT PCP TO RECOMMEND QUANTITATIVE GALT LEVELS TO HELP MAKE THAT DETERMINATION.
03/ /2015	LLAMMEREE	LM FOR CARRIE, NURSE TO CALL BACK.
03/ /2015	LLAMMEREE	RECEIVED CALL BACK FROM CARRIE, RN AT PCP OFFICE. REPORTED THAT REPEAT NBS IS SHOWING GALT ENZYME IS REDUCED AND GALACTOSE WNL. IT IS POSSIBLE INFANT IS A CARRIER FOR GALACTOSEMIA OR MAY HAVE A MILD VARIANT CALLED DUARTE. RECOMMENDED QUANTITATIVE GALT (GALACTOSE 1 PHOSPHATE URIDYL TRANSFERASE) LEVEL TO HELP DETERMINE IF A CARRIER OR DUARTE. IF PCP PREFERS, WE CAN FACILITATE REFERRAL TO GENETICS FOR THIS FOLLOW UP TESTING. CARRIE REPORTED INFANT IS DOING WELL. FAXED QUANTITATIVE GALT ORDERING INFO TO PCP OFFICE ALONG WITH WORKSHEET. 240-462-

Case 2: Logan

You call Logan's parents who confirm he's well; no vomiting, fever or changes in behavior. 2-3 oz. breast milk or regular formula q 2-3 hours. After explaining NBS result, **what do you tell them to do next?**

A. You will no longer be able to breastfeed because your child has galactosemia.
B. Switch to soy formula immediately until we can collect further testing.
C. Return immediately for a repeat further testing.

Case 2: Logan

State of Maryland
Department of Health and Mental Hygiene
Laboratories Administration
201 West Preston Street
Baltimore, Maryland 21201
Lawrence J. Hogan, Jr., Governor - Van T. Mitchell, Secretary
Robert Myers, Ph.D., Director

Maryland Newborn Screening Follow-Up Program
Telephone Number: **443.681.3916**
FAX Number:

CAPITOL MEDICAL GROUP
8401 CONNECTICUT AVENUE
CHEVY CHASE, MD [redacted] 1-301-907-

Genetic Evaluation: Childrens National Medical Center

State PID:	Perm. Name: / Birth Name:	Birth Date	Sex	Weight	Gest. Age	Birth Hosp.	Date Followup
		/2015	M		36		03/ /2015

Mother:

Certified Letter Date:

03/ /2015	LLAMMEREE	SPOKE WITH PCP OFFICE ASKING IF REPEAT NBS HAS BEEN COLLECTED. NURSE WILL NEED TO CALL BE BACK.
03/ /2015	LLAMMEREE	RECEIVED CALL BACK FROM NURSE CARRIE AT PCP OFFICE. SHE REPORTED INFANT IS DOING WELL AND REPEAT NBS WAS COLLECTED 03/17/2015 AND MAILED. WILL WATCH FOR REPEAT SPECIMEN.
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Case 2: Logan

You call Logan's parents who confirm he's well; no vomiting, fever or changes in behavior. 2-3 oz. breast milk or regular formula q 2-3 hours. After explaining NBS result, **what do you tell them to do next?**

A. You will no longer be able to breastfeed because your child has galactosemia.

B. Switch to soy formula immediately until we can collect further testing.

C. Return immediately for a repeat further testing.

Children's National

Galactosemia

Deficiency of Galactose-1-Phosphate Urdiyltransferase **(GALT) Enzyme**

- Responsible for processing galactose
- →Build-up of toxic galactose compounds

Symptoms

- Poor feeding
- Jaundice
- Vomiting/diarrhea
- Lethargy
- Fever

Typical Onset: DOL 3 or 4

Galactosemia Screening

TWO Analytes (typically):

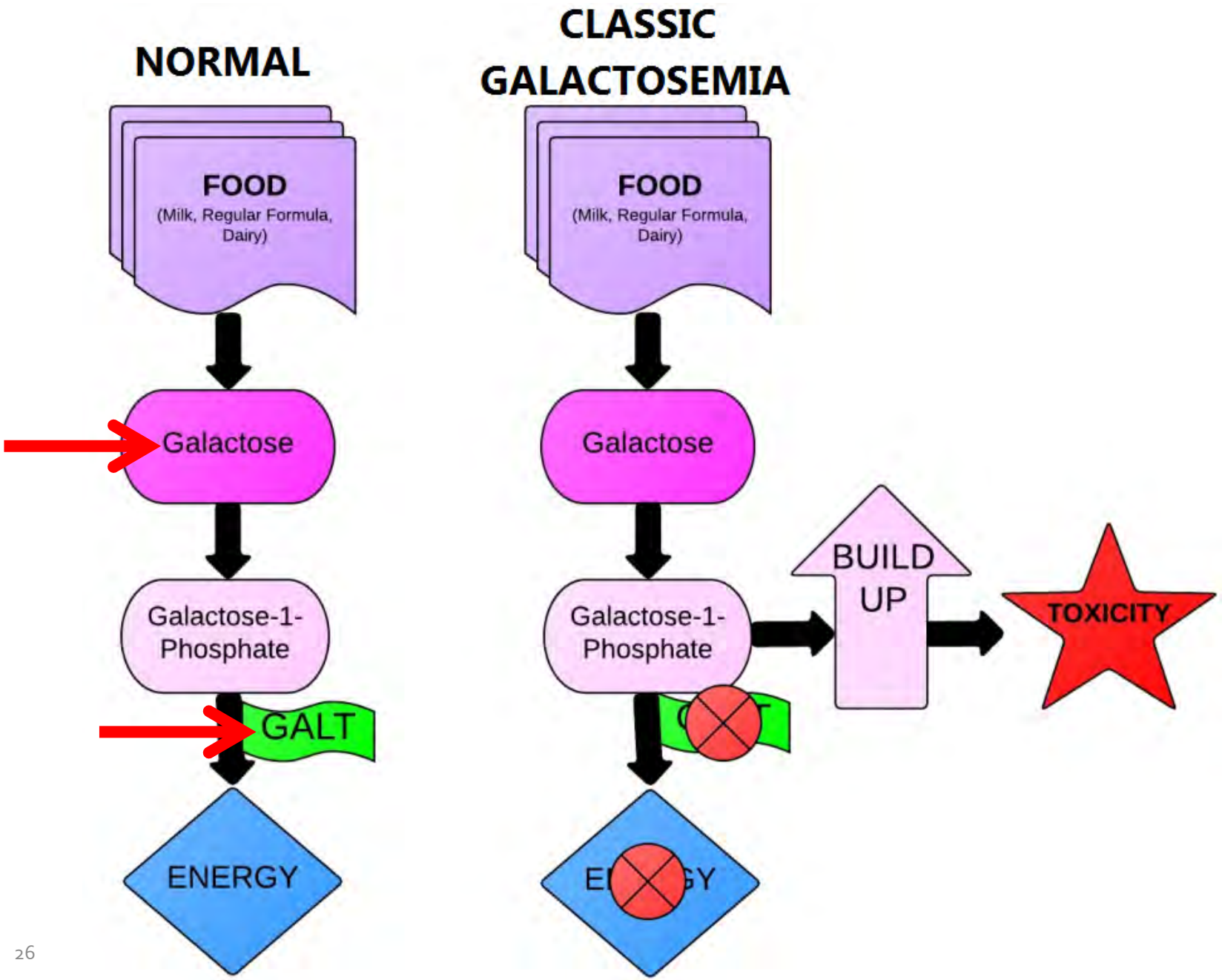
- Galactose-1-Phosphate-Uridyltransferase (GALT)
- Galactose and/or galactose-1-phosphate **(*Toxic*)**

Abnormal GALT ⬇

- Classic galactosemia
- Duarte variant galactosemia
- Classic galactosemia carrier
- False positive (heat!)

Abnormal galactose/galactose-1-phosphate ⬆

- Classic galactosemia
- Other variant galactosemia


NORMAL
FOOD
(Milk, Regular Formula, Dairy)
Galactose
Galactose-1-Phosphate
GALT
ENERGY
CLASSIC GALACTOSEMIA
FOOD
(Milk, Regular Formula, Dairy)
Galactose
Galactose-1-Phosphate
BUILD UP
TOXICITY

Galactosemia Screening

Abnormal GALT + galactose = CRITICAL

- Classic galactosemia
- Duarte variant galactosemia

IMMEDIATE galactose-restriction

- NO breast feeding
- NO regular formula
- Soy or hydrolyzed formula only

Galactosemia Screening

Confirmatory Testing

- Galactose-1-Phosphate
  - Toxic metabolite!
- GALT Enzyme
  - 0% = Classic galactosemia
  - 25% of normal = Duarte variant galactosemia
  - 50% of normal = likely carrier of galactosemia
- GALT Gene Sequencing

Case 3: Garth

PATIENT DATA			FILTER PAPER DATA			SUBMITTER DATA	
Name:			Filter Paper:			Submitter:	Providence Hospital
AKA Name:			Accession No:				1150 Varnum Street, NE
Birth Date:	01/07/	19:06	Date Collected:	01/09/20	05:10		Washington DC 20017
Sex:	F		Date Recvd:	01/10/20			
Weight (g):	2885		Transfused:				
Gestation:	39 weeks		Trans Date:	00/00/0000			
Med. Rec.			Completed:	01/13/20			
PS ID:			Print Date:	01/13/20		Physician:	

Propionylcarnitine (C3) = 12.05 µmol/L (Normal < 4.00 µmol/L)
Propionylcarnitine/Palmitoylcarnitine (C3/C16) ratio = 4.05 (Normal < 2.20)

Acylcarnitine Profile

Carnitine Uptake Deficiency

Result: PRESUMPTIVE POSITIVE

Propionylcarnitine (C3) = 12.05 µmol/L (Normal < 4.00 µmol/L)
Propionylcarnitine/Palmitoylcarnitine (C3/C16) ratio = 4.05 (Normal < 2.20)

The concentration of Propionylcarnitine (C3) and other indices such as the relative ratios of C3 to Acetylcarnitine (C2) or C3 to Palmitoylcarnitine (C16) were substantially above normal. The possible causes are Propionic Acidemias, Methylmalonic Acidemias, Cobalamin Defects, or Vitamin B12 Deficiency. We urgently recommend an organic acid analysis of urine and another dried filter paper blood specimen as well as a referral to a metabolic specialist.

DNA analysis detected no copies of the common Propionic Acidemia alleles E168K, 1218del 14/ins 12, 1170 insT, or Methylmalonic Acidemia alleles N219Y, G717V. Depending on population, these Propionic Acidemia mutations can account for up to 50% of the mutations that cause disease, while most Methylmalonic Acidemia mutations are private and family specific.

Genetic analysis for the Propionic Acidemia alleles E168K, 1218del 14/ins 12, 1170 insT, and the Methylmalonic Acidemia alleles N219Y, G717V are performed using polymerase chain reaction and melting curve analysis to detect the mutant and wild type forms of the gene. These disorders are inherited as autosomal recessive traits.

Case 3: Garth

6 day old male

PMHx

- Born at 39 weeks GA, C-section
- ABO incompatibility, history of jaundice with phototherapy x 48 hours
- Discharged DOL 4, breast and formula feeding

In the office

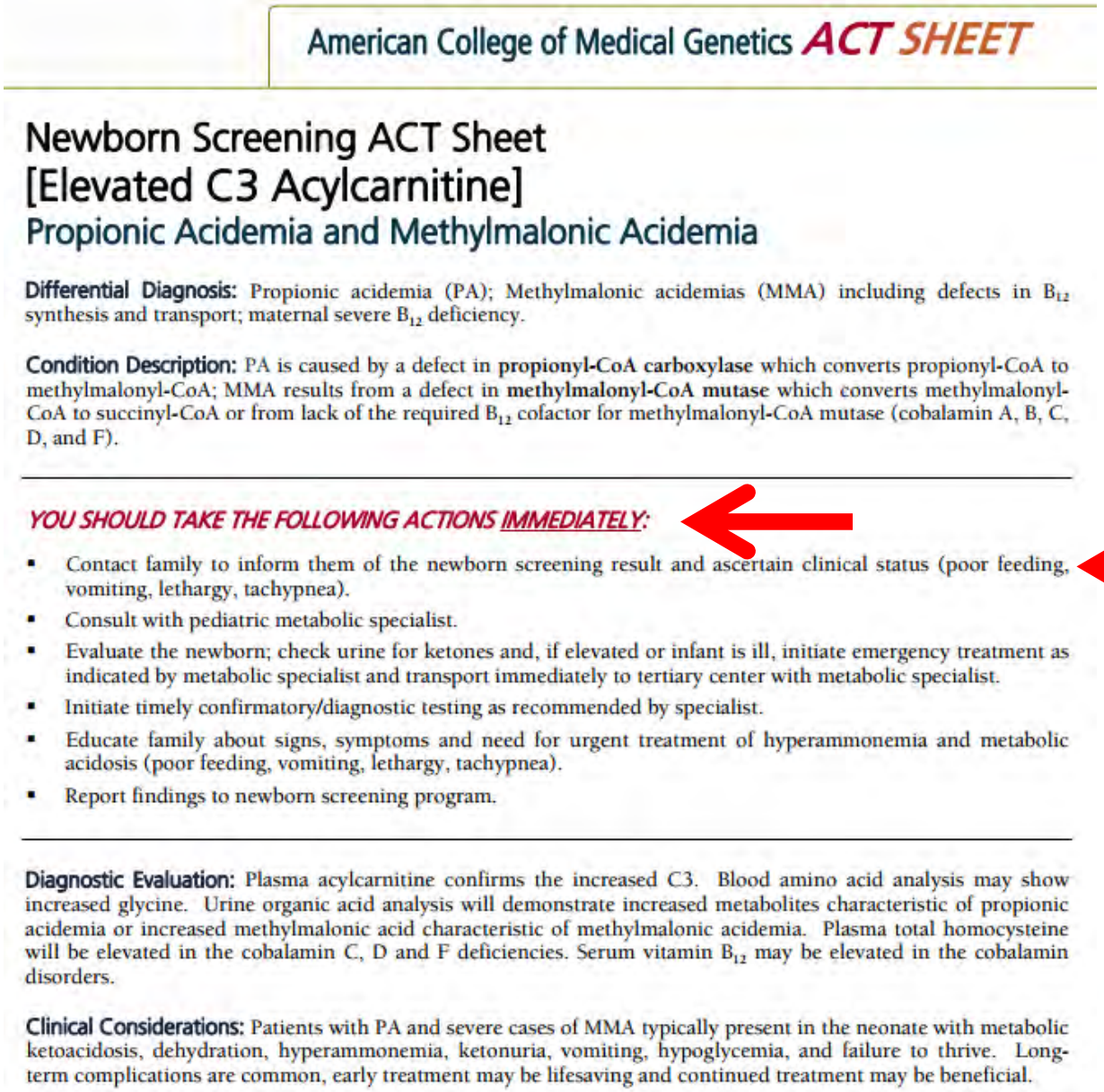
- Well appearing, jaundiced to the nipples
- Mom describes "maybe he's been eating a little less"

Case 3: Garth

After attempting to contact the metabolic specialist for several hours you have not heard back. It's nearing the end of the day, **what do you do next?**

A. Send this child to the emergency room.
B. Send the family home with careful instructions to go to the ER for any concerning signs/symptoms. Try the specialist again tomorrow.
C. Send the family home. Tell them to contact the metabolic specialist to schedule an appointment as soon as possible.

RESOURCE: ACMG ACT Sheets



American College of Medical Genetics **ACT SHEET**

Newborn Screening ACT Sheet
[Elevated C3 Acylcarnitine]
Propionic Acidemia and Methylmalonic Acidemia

Differential Diagnosis: Propionic acidemia (PA); Methylmalonic acidemias (MMA) including defects in B_{12} synthesis and transport; maternal severe B_{12} deficiency.

Condition Description: PA is caused by a defect in **propionyl-CoA carboxylase** which converts propionyl-CoA to methylmalonyl-CoA; MMA results from a defect in **methylmalonyl-CoA mutase** which converts methylmalonyl-CoA to succinyl-CoA or from lack of the required B_{12} cofactor for methylmalonyl-CoA mutase (cobalamin A, B, C, D, and F).

YOU SHOULD TAKE THE FOLLOWING ACTIONS IMMEDIATELY:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn; check urine for ketones and, if elevated or infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport immediately to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Educate family about signs, symptoms and need for urgent treatment of hyperammonemia and metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea).
- Report findings to newborn screening program.

Diagnostic Evaluation: Plasma acylcarnitine confirms the increased C3. Blood amino acid analysis may show increased glycine. Urine organic acid analysis will demonstrate increased metabolites characteristic of propionic acidemia or increased methylmalonic acid characteristic of methylmalonic acidemia. Plasma total homocysteine will be elevated in the cobalamin C, D and F deficiencies. Serum vitamin B_{12} may be elevated in the cobalamin disorders.

Clinical Considerations: Patients with PA and severe cases of MMA typically present in the neonate with metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Long-term complications are common, early treatment may be lifesaving and continued treatment may be beneficial.

Children's National

Case 3: Garth

After attempting to contact the metabolic specialist for several hours you have not heard back. It's nearing the end of the day, what do you do?

A. Send this child to the emergency room.
B. Send the family home with careful instructions to go to the ER for any concerning signs/symptoms. Try the specialist again tomorrow.
C. Send the family home. Tell them to contact the metabolic specialist to schedule an appointment as soon as possible.

Children's National

Organic Acid (OA) Conditions

Disorders of metabolism identifiable by specific urine metabolites

- Typically disordered amino acid (protein) metabolism

Symptoms

- Lethargy
- Feeding problems
- Ketonuria
- Can quickly progress to cerebral edema, coma, death

Onset: Variable

- Birth – early childhood

OA Screening

Analytes

- Acylcarnitines (denoted as C#)
  - Odd # chains (i.e. C_3, C_5DC)

Confirmatory Testing

- Urine organic acids
- +/- Acylcarnitines
- +/- Genetic testing

Case 4: Amanda

SEND TO: S-10574
INOVA FAIRFAX HOSPITAL
LABORATORY SERVICES BSMT
3300 GALLOWS RD
FALLS CHURCH VA 22042

Physician: FNA- NEONATOLOGIST
Hosp. of Birth: INOVA FAIRFAX HOSPITAL

Mother's Address:
HERNDON VA 20170

Tests performed	Normal Results	Result	Normal range
AMINO ACID PROFILE	Within normal limits		
Biotinidase Screen	Within Normal Limits		
CAH	Within Normal Limits		
Galactose Screen - Beutler Screen	Within Normal Limits		
Hemoglobinopathy Screen	Normal Newborn Hemoglobin		
IRT- Cystic Fibrosis	Within Normal Limts		
ORGANIC ACIDEMIA PROFILE	Within normal limits		
T4 PROFILE	Within normal limits		

Tests performed	Abnormal Results	Result		Normal range
ABNORMAL FATTY ACID OXIDATION				
C14:1	Above Normal Limits	.87	umol/L	< 0.66 umol/L
C14	Above Normal Limits	.85	umol/L	< 0.70 umol/L

INTERPRETATION: THE ABOVE RESULTS FOR FATTY ACID PROFILE ARE SUGGESTIVE OF POSSIBLE VLCAD.

Children's National

Case 4: Amanda

5 day old female

PMHx

- 37 weeks GA, C-section
- One episode of hypoglycemia in the nursery, resolved with oral feed

In the Office

- Well appearing
- Exclusive breastfeeding, 1-2 oz. q 3 hours

Case 4: Amanda

This is a trustworthy family and well-appearing child, is an immediate repeat newborn screen to rule out an FAOD appropriate in this case?

A. Yes

B. No

RESOURCE: NYMAC Diagnostic Guidelines

Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)
(Fatty Acid Oxidation Disorder)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD) 201475 237997005 / E71.310 Very long-chain acyl-CoA dehydrogenase 609575 / 1.3.99.13
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C14 53192-1 Elevated C14:1 53191-3
Initial Diagnostics at Referral Center	Plasma acylcarnitine profile Mutation analysis, as negative metabolites do not rule out the disorder
Recommended additional testing to consider at time of initial consultation	Blood glucose Plasma Carnitine, total and free Creatinine phosphokinase (CPK) Urine organic acids Liver function tests
Abnormal Metabolites Expected	Elevated C14, C14:1 Detection of known pathological mutations in trans Blood glucose depends on fed status of patient Normal/low carnitine levels CPK may be elevated in sick patients Urine organic acids are usually normal Liver function tests may be abnormal in sick patients

Case 4: Amanda

This is a trustworthy family and well-appearing child, is an immediate repeat newborn screen to rule out an FAOD appropriate in this case?

A. Yes

B. No

Repeat newborn screens are often NOT appropriate for fatty acid oxidation rule-out!

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Fatty Acid Oxidation Disorders (FAODs)

Deficiency of enzymes required to break down fat, leading to:

- Energy deficit
- Build-up of fatty acids

Symptoms

- Variable
- Sudden death*

Onset: variable

- Birth– adulthood

Fatty Acid Oxidation Disorders (FAODs)

Society for Inherited Metabolic Disorders
North American Metabolic Academy

FAO Disorder	Clinical Manifestations				
	Sudden death	Fasting Intolerance	Skeletal myopathy	Cardio - myopathy	Liver disease
Carnitine uptake defect					
LCFA transport/binding defect					
FA translocase deficiency					
CPT-I deficiency					
CACT deficiency					
CPT-II deficiency (neonatal)					
CPT-II deficiency (late onset)					
VLCAD deficiency					
ETF-QO deficiency (GA2)					
LCHAD deficiency					
TFP deficiency					
MCAD deficiency					
SCAD deficiency					
ETF deficiency					
Riboflavin responsive GA2					
M/SCHAD deficiency (SCHAD)					
MCKAT deficiency					
2,4-Dienoyl-CoA reductase def.					
HMG-CoA synthase deficiency					
HMG-CoA lyase deficiency					

FAOD Screening

Analytes

- Acylcarnitines (denoted as C#)
  - Even # chains (i.e. C8, C14:1)

Confirmatory Testing

- Plasma acylcarnitines
- Urine organic acids
- Free and total carnitine
- Genetic testing

Amino Acid Disorders (From Case 1, the smelly baby)

Disorders of specific amino acid metabolism

Symptoms: variable on metabolite

- MSUD: decreased feeding, lethargy progressing to encephalopathy, coma and death
- Phenylketonuria (PKU): intellectual disability

Onset: variable

- Birth– adulthood

Amino Acid Disorder Screening

Analytes

- Amino acids (i.e. phenylalanine, tyrosine)
- Not always primary markers
  - Methionine = Homocystinuria screen
  - Citrulline = Arginosuccinic aciduria screen

Confirmatory Testing

- Plasma amino acids

Case 5: Emily

New patient

- 6 month old female

PMHx

- Born in Central America, moved to U.S. one month ago
- Mom reports:
  - Birth history "normal", term, NSVD
  - Spitting up and reflux, resolved
  - No fevers, infections, major illnesses described

In the Office

- Well-appearing
- Developmental milestones appropriate for age

Case 5: Emily

There seems to be no record of this child ever having a newborn screen. With no specific concerns, what do you do next?

A. Continue to monitor for signs/symptoms of disease, but with no specific concerns do not order any further testing.
B. Collect and send a dried blood spot to your state newborn screening program.
C. Contact your state newborn screening program for assistance.

Case 5: Emily

There seems to be no record of this child ever having a newborn screen. With no specific concerns, what do you do next?

A. Continue to monitor for signs/symptoms of disease, but with no specific concerns do not order any further testing.

B. Collect and send a dried blood spot to your state newborn screening program.

C. Contact your state newborn screening program for assistance.

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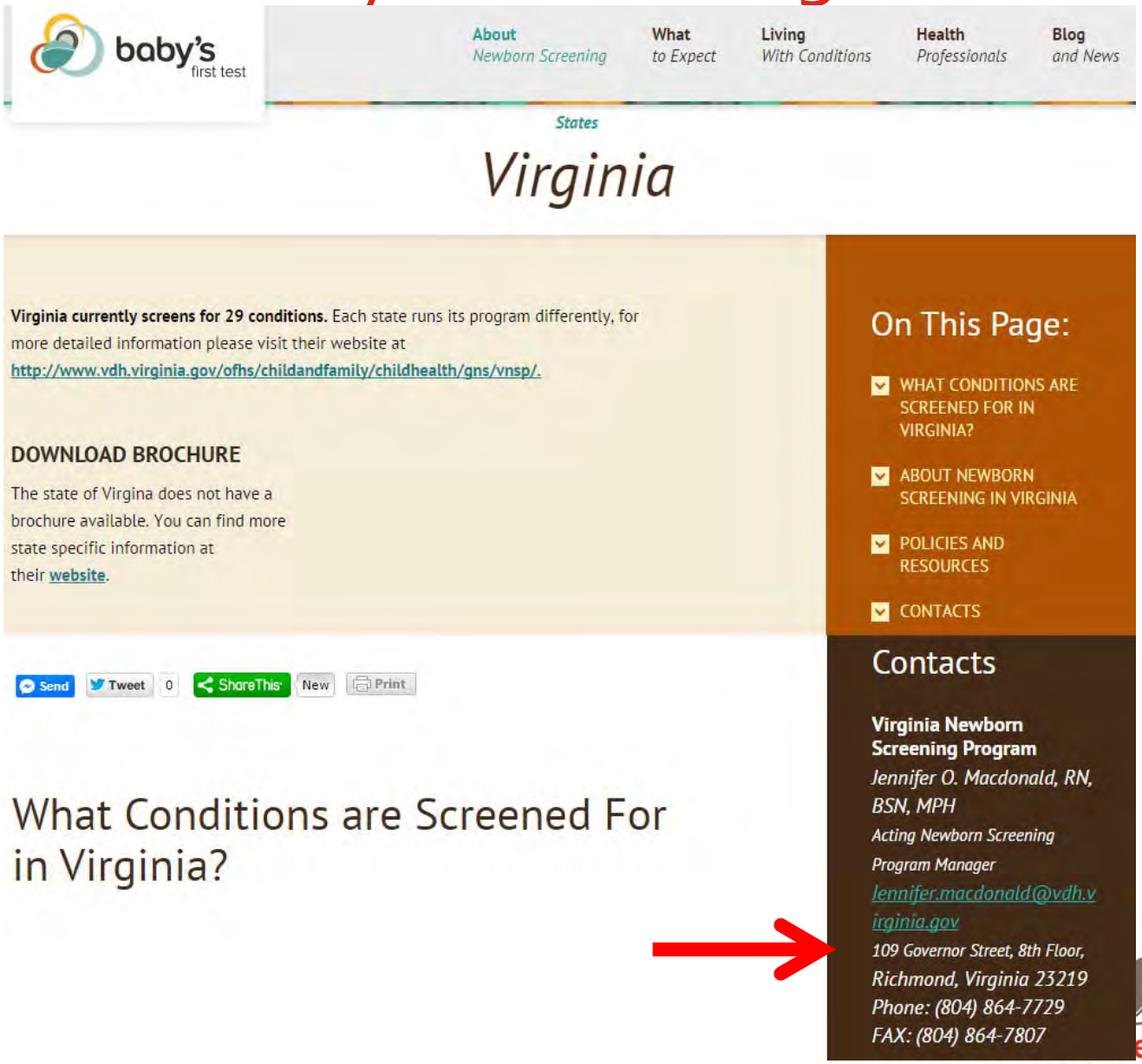
RESOURCE: babysfirsttest.org



NBS Resources

Children's National

Websites

ACT Sheets

http://www.ncbi.nlm.nih.gov/books/NBK55827/

Baby's First Test

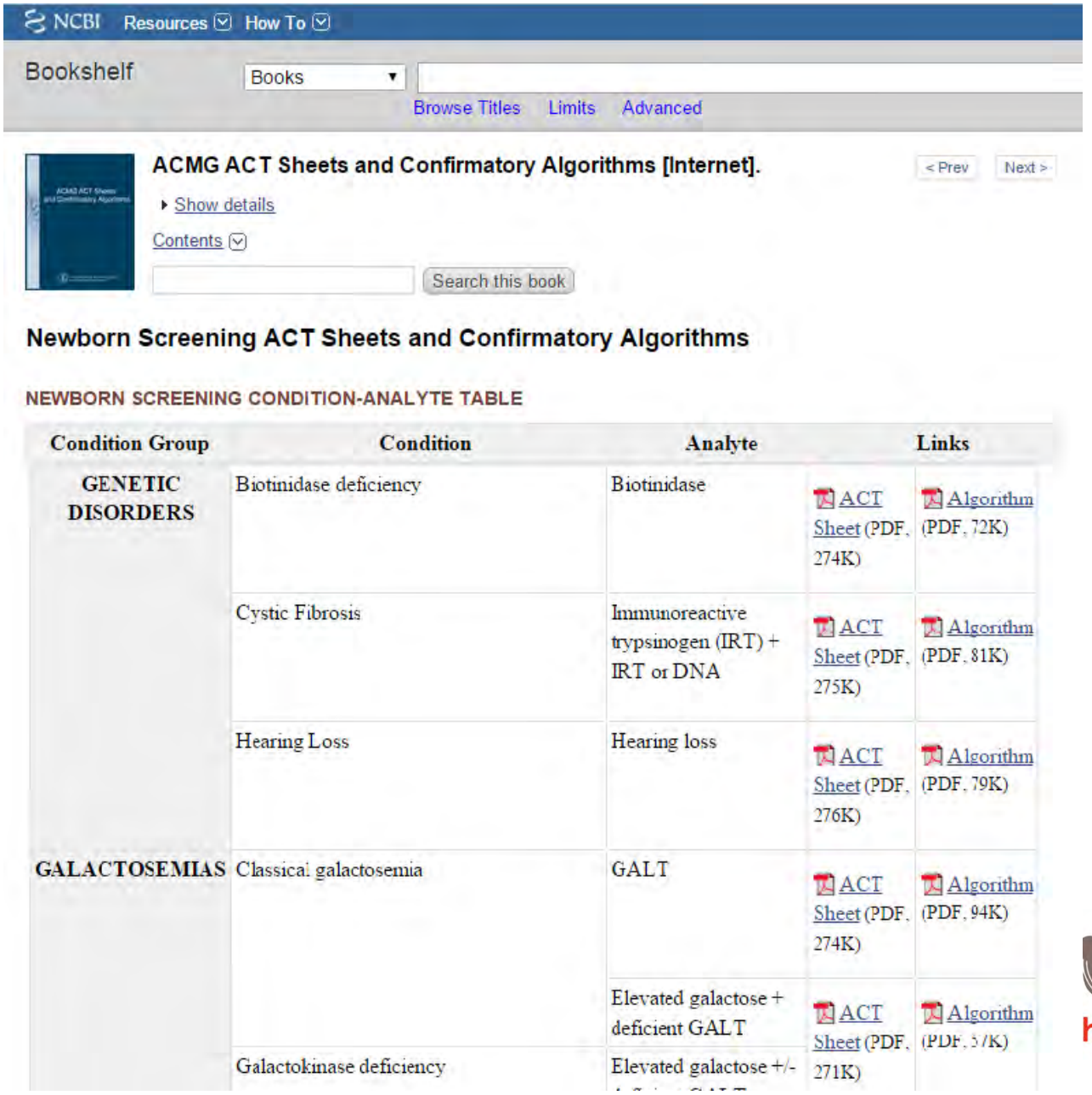
Babysfirsttest.org

NYMAC

http://www.wadsworth.org/newborn/nymac/NYMAC_Products.html

Diagnostic Guidelines:
http://www.wadsworth.org/newborn/nymac/docs/DX_Guidelines_2014-10-01.pdf

ACT Sheets



NCBI Resources How To

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ACMG ACT Sheets and Confirmatory Algorithms [Internet].

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Newborn Screening ACT Sheets and Confirmatory Algorithms

NEWBORN SCREENING CONDITION-ANALYTE TABLE

Condition Group	Condition	Analyte	Links	
GENETIC DISORDERS	Biotinidase deficiency	Biotinidase	ACT Sheet (PDF, 274K)	Algorithm (PDF, 72K)
	Cystic Fibrosis	Immunoreactive trypsinogen (IRT) + IRT or DNA	ACT Sheet (PDF, 275K)	Algorithm (PDF, 81K)
	Hearing Loss	Hearing loss	ACT Sheet (PDF, 276K)	Algorithm (PDF, 79K)
GALACTOSEMIAS	Classical galactosemia	GALT	ACT Sheet (PDF, 274K)	Algorithm (PDF, 94K)
		Elevated galactose + deficient GALT	ACT Sheet (PDF, 271K)	Algorithm (PDF, 57K)
	Galactokinase deficiency	Elevated galactose +/-		

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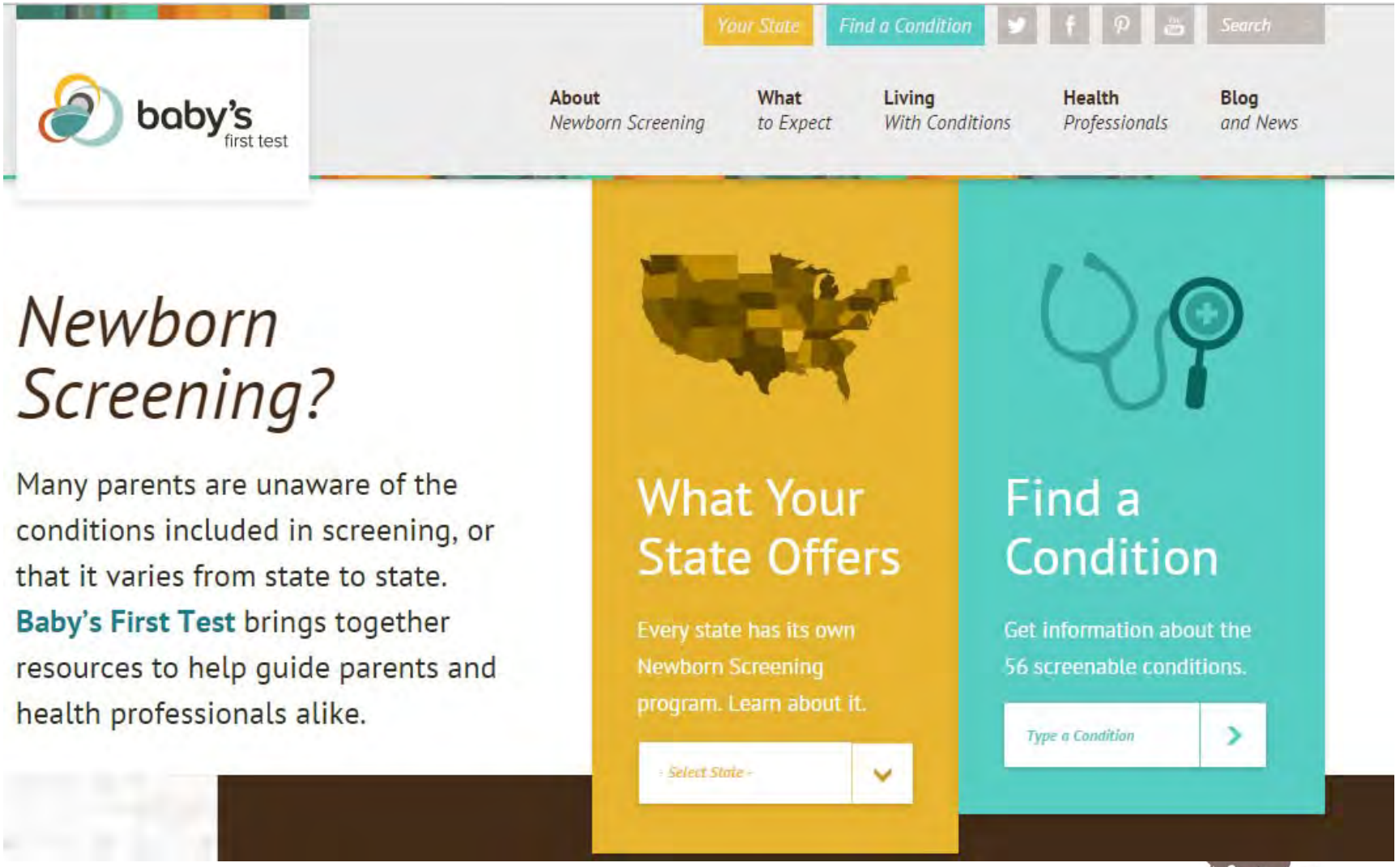
Baby's First Test



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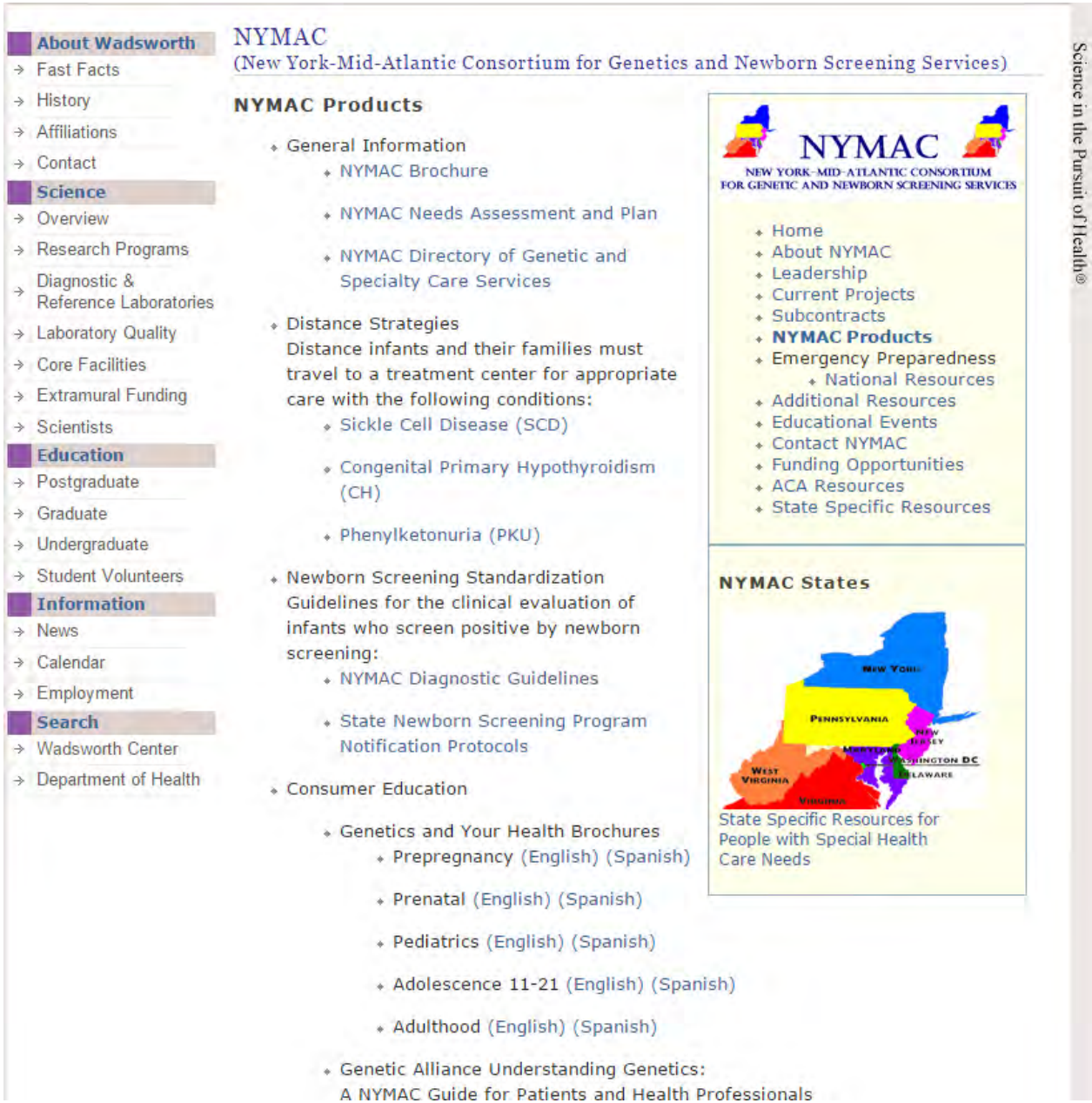

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NYMAC
(New York-Mid-Atlantic Consortium for Genetics and Newborn Screening Services)

NYMAC Products

- General Information
  - NYMAC Brochure
  - NYMAC Needs Assessment and Plan
  - NYMAC Directory of Genetic and Specialty Care Services
- Distance Strategies
  Distance infants and their families must travel to a treatment center for appropriate care with the following conditions:
  - Sickle Cell Disease (SCD)
  - Congenital Primary Hypothyroidism (CH)
  - Phenylketonuria (PKU)
- Newborn Screening Standardization
  Guidelines for the clinical evaluation of infants who screen positive by newborn screening:
  - NYMAC Diagnostic Guidelines
  - State Newborn Screening Program Notification Protocols
- Consumer Education
  - Genetics and Your Health Brochures
    - Prepregnancy (English) (Spanish)
    - Prenatal (English) (Spanish)
    - Pediatrics (English) (Spanish)
    - Adolescence 11-21 (English) (Spanish)
    - Adulthood (English) (Spanish)
  - Genetic Alliance Understanding Genetics:
    A NYMAC Guide for Patients and Health Professionals

NYMAC
NEW YORK-MID-ATLANTIC CONSORTIUM FOR GENETIC AND NEWBORN SCREENING SERVICES

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NYMAC States

State Specific Resources for People with Special Health Care Needs

Science in the Pursuit of Health®

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Last but not least…

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Take Home Points

NOT the "PKU Test"

Anxiety reduction

Use resources and support!

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References

CDC Grand Rounds: Newborn Screening and Improved Outcomes

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6121a2.htm

National Newborn Screening and Global Resource Center

http://genes-r-us.uthscsa.edu/

Secretary's Advisory Committee on Heritable Disorders in Newborns and Children Committee Report

http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/reportsrecommendations/reports/sachdnc2011report.pdf

Star-G: Screening, Technology and Research in Genetics

http://www.newbornscreening.info/index.html

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