

### Diagnostic Guidelines for Confirmation of Screen-Positive Newborn Screening Results

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#### Table of Contents

AbbreviationsAbbreviations	
Acid Sphingomyelinase (ASM) Deficiency	
Adrenal Hyperplasia, Congenital (CAH)	
Amino Acidemias	
Argininemia (ARG)	9
Argininosuccinic Aciduria (ASA) - aka Argininosuccinic Lyase Deficiency	
Argininosuccinic Lyase Deficiency - aka Argininosuccinic Aciduria (ASA)	
Beta-Ketothiolase Deficiency (BKT) - aka Beta-Oxothiolase Deficiency	
Beta-Oxothiolase Deficiency - aka Beta-Ketothiolase Deficiency (BKT)	
Biotinidase Deficiency (BIOT)	53
Carnitine-Acylcarnitine Translocase Deficiency (CACT)	22
Carnitine Palmitoyl Transferase Type Ia Deficiency (CPT-Ia)	
Carnitine Palmitoyl Transferase Type II Deficiency (CPT-II)	
Carnitine Uptake Defect (CUD) - aka Primary Carnitine Deficiency	23
Citrin Deficiency - aka Citrullinemia Type II (CIT-II)	
Citrullinemia Type I (CIT-I)	
Citrullinemia Type II (CIT-II) - aka Citrin Deficiency	
Classical Galactosemia (GALT)	
Cobalamin A,B Cofactor (Cbl A/B)	
Cobalamin C Cofactor Deficiency (Cbl C)	
Cobalamin D <sub>1</sub> Cofactor Deficiency (Cbl D <sub>1</sub> )	
Cobalamin D <sub>2</sub> Cofactor Deficiency (Cbl D <sub>2</sub> )	
Cobalamin F Cofactor Deficiency (Cbl F)	
Cobalamin J Cofactor Deficiency (Cbl J)	
Congenital Adrenal Hyperplasia (CAH)	
Congenital Hypothyroidism (CH)	
Cystic Fibrosis (CF)	54
2,4-Dienoyl-CoA Reductase Deficiency (2,4Di)	
Endocrinopathies	4-5
Ethylmalonic Encephalopathy (EMA)	
Fabry Disease	
Fatty Acid Oxidation Disorders	
Galactose Epimerase Deficiency (GALE)	5/
Galactokinase Deficiency (GALK)	
Galactosemia (Classical) (GALT)	
Galactosylceramide Beta-Galactosidase Deficiency	63
Gaucher Disease (GD)	
Glucocerebrosidase Deficiency	
Glucosylceramidase Deficiency, not including Saposin C Deficiency	
Glutaric Acidemia Type I (GA-I)	
Glusa con Stances Disease Time H (CSD II)	
Glycogen Storage Disease Type II (GSD II)	
Hemoglobin S/Beta <sup>0</sup> Thalassemia (HbS <sup>0</sup> )	
Hemoglobin S/Beta <sup>+</sup> Thalassemia (HbS <sup>+</sup> )	0
Hemoglobin SS (SS)	0
Hemoglobinopathies	
Hemoglobinopathies, Other	
Homocystinuria (HCY)	
Hunter Syndrome	
3-@Hydroxyacyl-Co-A Dehydrogenase Deficiency (HADH)	
4-Hydroxyphenylpyruvic Acid Oxidase Deficiency	
+-11 yurua yprich yrp yru yru Aciu Oaiuase Defricielle y	

3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG)	46
Hypermethioninemia (MET)	
Hyperphenylalaninemia (H-PHE)	16
Hypothyroidism, Primary Congenital (CH)	
Hypothyroidism, Secondary Congenital	
Isobutyryl-CoA Dehydrogenase Deficiency (IBCD)	35
Isobutyrylgylcinuria (IBG)	
Isovaleric Acidemia (IVA)	49
Krabbe Disease	
Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)	
Lysosomal Storage Disorders	
Malonic Aciduria (MAL)	
Maple Syrup Urine Disease (MSUD)	
Maroteaux-Lamy Syndrome (MPS VI)	66
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)	
Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT)	
Medium/Short-chain L-3-Hydroxyacyl-CoA Dehydrogenase Deficiency (M/SCHAD)	
Methionine Adenosyltransferase Deficiency	
2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase Deficiency (2M3HBA)	
2-Methylbutyryl Glycinuria (2-MBG)	
3-Methylcrotonyl-CoA Carboxylase Deficiency (3-MCC)	
3-Methylcrotonylglycinuria	
3-Methylglutaconic Aciduria Type I (3-MGA-I)	48
Methylmalonic Acidurias	36-39
Methylmalonyl-CoA Mutase Deficiency (MUT)	
Mucopolysaccharidosis Type I (MPS I)	
Mucopolysaccharidosis Type II (MPS II)	
Mucopolysaccharidosis Type VI (MPS VI)	
Multiple Acyl-CoA Dehydrogenase Deficiency (MADD)	
Multiple Carboxylase Deficiency (MCD)	
Niemann-Pick Syndrome, Types A, B	
Organic Acidemias	
Other Genetic Conditions	
Other Hemoglobinopathies	
Phenylketonuria (PKU)	
Pompe Disease	
Primary Carnitine Deficiency	23
Primary Congenital Hypothyroidism (CH)	5
Propionic Acidemia (PA)	
S-Adenosylhomocysteine Hydroxolase (SAH)	
Secondary Congenital Hypothyroidism	
Severe Combined Immune Deficiency (SCID)	
Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD)	29
Sickle Cell Carrier (HbAS)	
Sickle Cell Disease	
Sickle C Disease (HbSC)	
T-cell-related Lymphocyte Deficiencies	
Thyroxine-Binding Globulin Deficiency	
Trifunctional Protein Deficiency (TFP)	
Tyrosinemia Type I (TYR-I)	
Tyrosinemia Type II (TYR-II)	18
Tyrosinemia Type III (TYR-III)	19
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	
X-Linked Adrenoleukodystrophy (X-ALD)	67

### Congenital Adrenal Hyperplasia (CAH) (Endocrine Disorder)

Disease (common abbreviation)	Congenital Adrenal Hyperplasia (CAH) (non-classical; salt-
	wasting; simple virilizing)
MIM#	201910
SNOMED Code / ICD-10-CM Code	237754008; 71578002; 52604008 / E25.0
Enzyme or other abnormality	21-Hydroxylase
MIM # / Enzyme Commission #	201910 / 1.14.99.10
Abnormal Newborn Screening Metabolite(s)	Elevated 17-hydroxyprogesterone (17-OHP)
LOINC Number(s)	38473-5
	Serum 17-OHP
Initial Diagnostics at Referral Center	Serum electrolytes
	Blood glucose
	Clinical suspicion low: None
Recommended additional testing to consider	Clinical suspicion high:
at time of initial consultation	Steroid profile
at time of thittal consultation	ACTH stimulation test
	Mutation analysis
	Severe:
	Markedly elevated 17-OHP
Abnormal Metabolites Expected	Decreased sodium, increased potassium, low glucose
Abnormai Meiaboines Expeciea	Mild to moderate:
	Mild to moderate elevation in 17-OHP
	Electrolytes and glucose can be normal
If initial testing is negative has the disorder been ruled out?	Yes (only classical 21-hydroxylase deficiency CAH)*
	Markedly elevated 17-OHP is diagnostic of severe CAH
	Mild to moderate 17-OHP elevation do:
Diagnostic Confirmation	Steroid profile
	ACTH stimulation test
	Mutation analysis
Differential Diagnosis	Stress, prematurity
Specific Testing Laboratories as listed in	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0852654%5BDISCUI
Genetic Testing Registry	%5D&condition=C0852654&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1171/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/CAH.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	NBS_Elevated_17OHP.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

<sup>\*</sup> Please note that in some cases, the initial CAH screen may be negative. If this diagnosis is suspected on clinical grounds, please consult pediatric endocrinology. Also be aware that there are several other forms of CAH due to other enzyme deficiencies, as well as congenital forms of adrenal insufficiency, that are not detected by the screen.

#### Congenital Hypothyroidism (CH) including Primary Congenital Hypothyroidism, Secondary Congenital Hypothyroidism and Thyroxine-Binding Globulin Deficiency (Endocrine Disorder)

Disease (common abbreviation)	Primary Congenital Hypothyroidism (CH); Secondary Congenital Hypothyroidism; Thyroxine-Binding Globulin
	Deficiency
MIM #	Multiple genes or not genetic
SNOMED Codes / ICD-10-CM Codes	190268003; 82598004; 237544006 / E03.1; E03.1; E07.89
Enzyme or other abnormality	N/A
MIM # / Enzyme Commission #	N/A / N/A
•	Decreased thyroxine (T4)
Abnormal Newborn Screening Metabolite(s)	31144-9
LOINC Number(s)	Elevated thyroid stimulating hormone (TSH) 29575-8
Listing Discounting at Defense 1 Courter	T4
Initial Diagnostics at Referral Center	TSH
Recommended additional testing to consider at time of initial consultation	None
Abnormal Matabalitas Ernaatad	Low T4
Abnormal Metabolites Expected	Elevated TSH
If initial testing is negative has the disorder	Newborns who are ill or premature may experience a late rise in
been ruled out?	TSH so should be reevaluated **
	Repeat TSH, T4
Diagnostic Confirmation	Free T4
	T3 resin uptake
Differential Diagnosis	
Specific Testing Laboratories as listed in	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0010308%5BDISCUI
Genetic Testing Registry	%5D&condition=C0010308&compare_labs=1
GeneReviews	None
	Elevated TSH:
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Primary_TSH.pdf
Sheet	Low T4/Elevated TSH:
	www.acmg.net/StaticContent/ACT/Primary_T4_Followup.pdf
	Elevated TSH:
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-TSH.pdf
	Low T4/Elevated TSH:
0	www.acmg.net/StaticContent/ACT/Algorithms/Visio-CH-
	T4.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

<sup>\*\*</sup> Please be aware that secondary hypothyroidism due to hypopituitarism will present with low T4 and low TSH.

# Sickle Cell Disease including Hemoglobin SS (SS), Hemoglobin S/Beta<sup>+</sup> Thalassemia (HbSB<sup>+</sup>), Hemoglobin S/Beta<sup>0</sup> Thalassemia (HbSB<sup>0</sup>), and Sickle C Disease (HbSC) (Hemoglobinopathy)

Disease (common abbreviation)	Sickle Cell Disease including Hemoglobin SS (SS),
Disease (common abbreviation)	Hemoglobin S/Beta <sup>+</sup> Thalassemia (HbSß <sup>+</sup> ), Hemoglobin
	S/Beta <sup>0</sup> Thalassemia (HbSß <sup>0</sup> ) and Sickle C Disease (HbSC)
MIM #	603903 (SS); 141900 (Others)
SNOMED Code / ICD-10-CM Code	Multiple / Multiple
Enzyme or other abnormality	Beta globin
MIM # / Enzyme Commission #	MIM # 141900 / N/A
Abnormal Newborn Screening Metabolite(s)	FS, FSA, FSC, etc.
LOINC Number(s)	N/A
Initial Diagnostics at Referral Center	Hemoglobin electrophoresis or high performance liquid chromatography (HPLC)
Recommended additional testing to consider	CBC
at time of initial consultation	
	FS, FSA, FSC, etc.
Abnormal Metabolites Expected	CBC abnormalities may be expected depending on the disorder;
	newborn CBC normal in SS
If initial testing is negative has the disorder	Yes
been ruled out?	Hamadahin alaatranharasis or HDLC
Diagnostic Confirmation	Hemoglobin electrophoresis or HPLC
Differential Diagnosis	
	SS:
	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0002895%5BDISCUI
	%5D&condition=C0002895&compare_labs=1
Specific Testing Laboratories as listed in	HbSβ <sup>O</sup> , HbSβ <sup>+</sup> :
Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0221019%5BDISCUI
Geneue Testing Registry	%5D&condition=C0221019&compare_labs=1
	HbSC:
	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0019034%5BDISCUI
	%5D&condition=C0019034&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1377/
	HbSS, HbSβ <sup>0</sup> :
	www.acmg.net/StaticContent/ACT/ACT_sheet_HBSS_FS4.
	28.06%20ljo.pdf
American College of Medical Genetics ACT Sheet	HbSß <sup>+</sup> : www.acmg.net/StaticContent/ACT/ACT-
	sheet Hb Sbeta plus thal FSA.pdf
	HbSC: www.acmg.net/StaticContent/ACT/ACT-
	sheet_HBSC_FSC.pdf
American College of Medical Genetics Algorithm	All Hemoglobinopathies:
	wwww.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Hemoglobinopathy 4.18.06.pdf
Recommended Uniform Screening Panel	Core Panel
(RUSP)	

Other Hemoglobinopathies (Hemoglobinopathy)

Disease (common abbreviation)	Other Hemoglobinopathies
MIM#	141900
SNOMED Code / ICD-10-CM Code	Multiple / Multiple
Enzyme or other abnormality	Beta globin
MIM # / Enzyme Commission #	141900 / N/A
Abnormal Newborn Screening Metabolite(s)	FVar, etc.
LOINC Number	N/A
Initial Diagnostics at Referral Center	Hemoglobin electrophoresis or high performance liquid chromatography (HPLC)
Recommended additional testing to consider at time of initial consultation	CBC
Abnormal Metabolites Expected	FVar, etc.
Abnormai Meiaboines Expeciea	CBC abnormalities may be expected
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Hemoglobin electrophoresis or HPLC
Differential Diagnosis	
Specific Testing Laboratories as listed in Genetic Testing Registry	Multiple labs; see Sickle Cell Disease
GeneReviews	See Sickle Cell Disease
American College of Medical Genetics ACT Sheet	See Sickle Cell Disease
American College of Medical Genetics	All Hemoglobinopathies:
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Hemoglobinopathy_4.18.06.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

### Sickle Cell Carrier (HbAS) (Hemoglobinopathy)

	Sights Call Coming (IIIA S)
Disease (common abbreviation)	Sickle Cell Carrier (HbAS)
MIM#	141900
SNOMED Code / ICD-10-CM Code	Multiple / Multiple
Enzyme or other abnormality	Beta globin
MIM # / Enzyme Commission #	141900 / N/A
Abnormal Newborn Screening Metabolite(s)	FAS
LOINC Number(s)	N/A
Initial Diagnostics at Referral Center	Hemoglobin electrophoresis or high performance liquid chromatography (HPLC)
Recommended additional testing to consider at time of initial consultation	СВС
Abnormal Metabolites Expected	FAS Newborn CBC normal
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Hemoglobin electrophoresis or HPLC
Differential Diagnosis	
Specific Testing Laboratories as listed in Genetic Testing Registry	See Sickle Cell Disease
GeneReviews	See Sickle Cell Disease
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/ACT_sheet_Hb_carrier_trai
Sheet	t_FAS.pdf
A	All Hemoglobinopathies:
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Hemoglobinopathy_4.18.06.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

### Argininemia (ARG) (Amino Acidemias)

Disease (common abbreviation)	Argininemia (ARG)
MIM#	207800
SNOMED Code / ICD-10-CM Code	23501004 / E72.21
Enzyme or other abnormality	Arginase
MIM # / Enzyme Commission #	608313 / 3.5.3.1
Abnormal Newborn Screening Metabolite(s) LOINC Number	Elevated arginine 47562-4
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
Recommended additional testing to consider	Liver function tests
at time of initial consultation	Ammonia
at time of initial consultation	Urine orotic acid
	Elevated arginine (PAA)
Abnormal Metabolites Expected	Normal liver function tests expected
Tionormai Metabolites Expected	Normal/slightly elevated ammonia
	Normal/elevated orotic acid
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Elevated arginine
Diagnostic Confirmation	RBC arginase assay if available
Differential Diagnosis	None
Specific Testing Laboratories as listed in	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268548%5BDI
Genetic Testing Registry	SCUI%5D&condition=C0268548&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1159/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/Arginine.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Arginine.pdf
Recommended Uniform Screening Panel	Zigmino-pui
(RUSP)	Secondary Target
(RODI)	

#### Argininosuccinic Lyase Deficiency; Argininosuccinic Aciduria (ASA) (Amino Acidemia)

mino Acidemia)
Argininosuccinic Lyase Deficiency; Argininosuccinic Aciduria
(ASA)
207900
41013004 / E72.22
Argininosuccinic lyase
608310 / 4.3.2.1
Elevated citrulline (some states elevated ASA)
42892-0
Plasma amino acids (PAA)
Urine orotic acid
Liver function tests
Ammonia
Elevated citrulline, glutamine, and argininosuccinic acid (PAA)
Decreased arginine (PAA)
Elevated urine orotic acid possible
Normal liver function tests expected
Elevated ammonia expected
Yes
105
Elevated argininosuccinic acid
Citrullinemia Type I (CIT I); Citrullinemia Type II (CIT
II)/Citrin Deficiency
www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268547%5BDISCUI
%5D&condition=C0268547&compare_labs=1
www.ncbi.nlm.nih.gov/books/NBK51784/
www.coma.not/StaticContant/ACT/Citmillinomic.adf
www.acmg.net/StaticContent/ACT/Citrullinemia.pdf
www.acmg.net/StaticContent/ACT/Algorithms/Visio-
<u>Citrulline.pdf</u>
Core Panel

### Citrullinemia Type I (CIT-I) (Amino Acidemia)

(Alimio Actucina)		
Disease (common abbreviation)	Citrullinemia Type I (CIT-I)	
MIM #	215700	
SNOMED Code / ICD-10-CM Code	398680004 / E72.23	
Enzyme or other abnormality	Argininosuccinate synthetase	
MIM # / Enzyme Commission #	603470 / 6.3.4.5	
Abnormal Newborn Screening Metabolite(s)	Elevated citrulline	
LOINC Number	42892-0	
List al Digger acting at Referred Conton	Plasma amino acids (PAA)	
Initial Diagnostics at Referral Center	Urine orotic acid	
Recommended additional testing to consider	Liver function tests	
at time of initial consultation	Ammonia	
	Elevated citrulline(and alanine and glutamine if sick) (PAA)	
	Decreased arginine (PAA)	
Abnormal Metabolites Expected	Elevated urine orotic acid	
	Normal liver function tests expected	
	Elevated ammonia expected	
If initial testing is negative has the disorder been ruled out?	Yes	
	Elevated citrulline, (and alanine and glutamine if sick) and	
	orotic acid levels	
Diagnostic Confirmation	Enzyme analysis in fibroblasts	
, v	Mutation analysis is required to differentiate between mild CIT	
	Type I and Citrin Deficiency	
Differential Diagnosis	Argininosuccinic Lyase Deficiency/ Argininosuccinic Aciduria (ASA); Citrullinemia Type II (CIT II)/Citrin Deficiency	
Specific Testing Laboratories as listed in	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0175683%5BDISCUI	
Genetic Testing Registry	%5D&condition=C0175683&compare labs=1	
<u> </u>		
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1458/	
American College of Medical Genetics ACT	ywww.aama.nat/StatiaContant/ACT/Citmillinamis.adf	
Sheet	www.acmg.net/StaticContent/ACT/Citrullinemia.pdf	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-	
Algorithm	<u>Citrulline.pdf</u>	
Recommended Uniform Screening Panel (RUSP)	Core Panel	

### Citrullinemia Type II (CIT-II); Citrin Deficiency) (Amino Acidemia)

Disease (common abbreviation)	Citrullinemia Type II (CIT-II); Citrin Deficiency
MIM #	603471, 605814
SNOMED Code / ICD-10-CM Code	30529005 / E72.23
Enzyme or other abnormality	Mitochondrial aspartate-glutamate carrier (citrin)
MIM # / Enzyme Commission #	603859 / None
Abnormal Newborn Screening Metabolite(s)	Elevated citrulline
LOINC Number(s)	42892-0
	Plasma amino acids (PAA)
Initial Diagnostics at Referral Center	Urine orotic acid
Recommended additional testing to consider	Liver function tests
at time of initial consultation	Ammonia
at time of initial consultation	RBC Galactose-1-Phosphate
	Elevated citrulline, arginine, methionine, threonine and lysine
	(PAA)
Abnownal Metabolitas Expected	Elevated urine orotic acid possible
Abnormal Metabolites Expected	Liver function tests: elevated bilirubin
	Normal ammonia
	Elevated RBC galactose-1-phosphate
If initial testing is negative has the disorder	Yes
been ruled out?	Yes
	Elevated citrulline with normal ammonia and glutamine levels
Diagnostic Confirmation	Mutation analysis is required to differentiate between mild CIT
V	Type I and Citrin Deficiency
D:00 (1 D)	Argininosuccinic Lyase Deficiency/ Argininosuccinic Aciduria
Differential Diagnosis	(ASA); Citrullinemia Type I (CIT I)
Specific Testing Laboratories as listed in	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1863844%5BDISCUI
Genetic Testing Registry	%5D&condition=C1863844&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1181/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Citrullinemia.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	<u>Citrulline.pdf</u>
Recommended Uniform Screening Panel (RUSP)	Secondary Target

Note: Several cases of citrin deficiency are detected on second screen, with a completely normal first screen

### Homocystinuria (HCY) (Amino Acidemia)

(-	(Allinio Actucina)	
Disease (common abbreviation)	Homocystinuria (HCY)	
MIM #	236200	
SNOMED Code / ICD-10-CM Code	24308003 / E72.11	
Enzyme or other abnormality	Cystathionine beta-synthase (CBS)	
MIM # / Enzyme Commission #	236300 / 4.2.1.22	
Abnormal Newborn Screening Metabolite(s)	Elevated methionine	
LOINC Number(s)	47700-0	
	Plasma amino acids (PAA)	
Initial Diagnostics at Referral Center	Total plasma homocysteine	
	Urine organic acids (UOA)	
Recommended additional testing to consider at time of initial consultation	Liver function tests	
	Elevated methionine, free homocystine and total homocysteine	
Abnormal Motabolitas Ernaatad	(PAA)	
Abnormal Metabolites Expected	No succinylacetone (UOA)	
	Normal liver function tests expected	
If initial testing is negative has the disorder been ruled out?	Yes	
Diamondia Carifornia	Elevated methionine, free homocystine and total homocysteine	
Diagnostic Confirmation	Evaluate for B6 responsiveness and/or do mutation analysis	
Differential Diagnosis	Hypermethioninemia (HMET)/Tyrosinemia Type I (TYR I)/Liver Disease	
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C3150344%5BDISCUI	
Genetic Testing Registry	%5D&condition=C3150344&compare_labs=1	
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1524/	
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/Methionine.pdf	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-	
Algorithm	Methionine.pdf	
Recommended Uniform Screening Panel (RUSP)	Core Panel	

### Hypermethioninemia (MET); Methionine Adenosyltransferase Deficiency; S-Adenosylhomocysteine Hydrolase (SAH)

(Amino Acidemia)

Disease (common abbreviation)	Hypermethioninemia (MET); S-Adenosylhomocysteine
	Hydrolase (SAH); Methionine Adenosyltransferase Deficiency
MIM #	250850
SNOMED Code / ICD-10-CM Code	37695001 / E72.19
Enzyme or other abnormality	Methionine adenosyltransferase (MAT I/II)
MIM # / Enzyme Commission #	601468 / 2.5.1.6
Abnormal Newborn Screening Metabolite(s)	Elevated methionine
LOINC Number(s)	47700-0
	Plasma amino acids
Initial Diagnostics at Referral Center	Total plasma homocysteine
	Urine organic acids
Recommended additional testing to consider at time of initial consultation	Liver function tests
	Elevated methionine
Abnormal Metabolites Expected	Normal/elevated total homocysteine
	Normal organic acid analysis
If initial testing is negative has the disorder been ruled out?	Yes
	Persistently elevated methionine
Diagnostic Confirmation	Measurement of S-adenosylhomocysteine, S-
	adenosylmethionine and sarcosine in plasma
Differential Diagnosis	Homocystinuria (HCY); Liver Disease
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268621%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268621&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Methionine.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	<u>Methionine.pdf</u>
Recommended Uniform Screening Panel (RUSP)	Secondary Target

### Maple Syrup Urine Disease (MSUD) (Amino Acidemia)

Disease (common abbreviation)	Maple Syrup Urine Disease (MSUD)
MIM#	248600
SNOMED Code / ICD-10-CM Code	27718001 / E71.0
Enzyme or other abnormality	Branched-chain alpha-keto acid dehydrogenase (BCKD)
MIM # / Enzyme Commission #	608348 / 1.2.4.4
Abnormal Newborn Screening Metabolite(s)	Elevated leucine + isoleucine
LOINC Number(s)	53152-5
L'' 1D' D' LC	Plasma amino acids (PAA)
Initial Diagnostics at Referral Center	Urine organic acids (UOA)
Recommended additional testing to consider at time of initial consultation	Urine ketones
	Elevated leucine, isoleucine, valine and alloisoleucine (PAA)
Abnormal Metabolites Expected	Abnormal branched-chain ketoacids (UOA)
•	Elevated urinary ketones
If initial testing is negative has the disorder been ruled out?	Yes
	Elevated branched-chain amino acids and elevated
Diagnostic Confirmation	alloisoleucine
Diagnostic Confirmation	Consider BCKD assay in cultured fibroblasts in mild cases with
	intermittent or mild elevations of branched chain amino acids.
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0024776%5BDISCUI
Genetic Testing Registry	%5D&condition=C0024776&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1319/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Leucine.pdf
Sheet	vvvvv ome not/StaticContent/ACT/Alcorithme/Visio
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	<u>Leucine.pdf</u>
Recommended Uniform Screening Panel (RUSP)	Core Panel

### Phenylketonuria (PKU) and Hyperphenylalaninemia (H-PHE) (Amino Acidemia)

Disease (common abbreviation)	Phenylketonuria (PKU) and Hyperphenylalaninemia (H-PHE)
MIM#	261600
SNOMED Code / ICD-10-CM Code	7573000 / E70.0
Enzyme or other abnormality	Phenylalanine hydroxylase
MIM # / Enzyme Commission #	261600 / 1.14.16.1
Abnormal Newborn Screening Metabolite(s)	Elevated phenylalanine
LOINC Number(s)	29573-3
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
Recommended additional testing to consider	Urine biopterin and neopterin
at time of initial consultation	Dihydropteridine reductase activity
	Elevated phenylalanine levels
Abnormal Metabolites Expected	Normal/low tyrosine (PAA)
	Normal pterin studies
If initial testing is negative has the disorder	Yes
been ruled out?	168
Diagnostic Confirmation	Elevated phenylalanine levels
Differential Diagnosis	Defects of Biopterin Metabolism, Neonates on Total Parenteral
2 typer entitled 2 tag the site	Nutrition (TPN)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0031485%5BDISCUI
Genetic Testing Registry	%5D&condition=C0031485&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1504/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Phenylalanine.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	<u>Phenylalanine.pdf</u>
Recommended Uniform Screening Panel	Core Panel
(RUSP)	

### Tyrosinemia Type I (TYR-I) (Amino Acidemia)

	Allinio Acidenia)
Disease (common abbreviation)	Tyrosinemia Type I (TYR-I)
MIM#	276700
SNOMED Code / ICD-10-CM Code	410056006 / E70.21
Enzyme or other abnormality	Fumarylacetoacetase hydrolase (FAH)
MIM # / Enzyme Commission #	276700 / 3.7.1.2
	Elevated tyrosine(tyrosine may be normal at the time of the first
Abrama al Naula ama Canagaire a Matabalita(a)	screen)
Abnormal Newborn Screening Metabolite(s)	35571-9
LOINC Number(s)	Elevated succinylacetone
	53231-7
	Plasma amino acids (PAA)
Initial Diagnostics at Referral Center	Urine organic acids (UOA) including succinylacetone
	Liver function tests
Recommended additional testing to consider	A1.1 C
at time of initial consultation	Alpha fetoprotein
,	Elevated tyrosine, methionine (PAA)
	Elevated succinylacetone and succinylacetoacetate (UOA)
Abnormal Metabolites Expected	Liver function tests may be abnormal in sick patients
	Elevated alpha fetoprotein
If initial testing is negative has the disorder	•
been ruled out?	Yes
Diagnostic Confirmation	Presence of succinylacetone is diagnostic
	Tyrosinemia Type II (TYR II); Tyrosinemia Type III (TYR III),
Differential Diagnosis	Total Parenteral Nutrition (TPN), Transient Tyrosinemia of
	the Newborn
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268490%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268490&compare_labs=1
Specific Testing Laboratories as listed in the	1000
Genetic Testing Registry	
, ,	www.gobi.glas.gib.com/bools/NDV1515/
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1515/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Tyrosine.pdf
Sheet	www.acmg.net/StaticContent/ACT/Tyrosme.pui
American College of Madical Caretia	Tyrosine normal/elevated; succinylacetone elevated:
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Tyrosine normal or elevated and SUAC elevated DM.pdf
Recommended Uniform Screening Panel	
(RUSP)	Core Panel
( /	

#### Tyrosinemia Type II (TYR-II) (Amino Acidemia)

Disease (common abbreviation)  MIM # 276600  \$NOMED Code / ICD-10-CM Code   Enzyme or other abnormality   Abnormal Newborn Screening Metabolite(s)   LOINC Number(s)   LOINC Number(soit)   L	( <i>I</i>	Amino Acidemia)
Abnormal Newborn Screening Metabolites   Signature of the commendation	Disease (common abbreviation)	Tyrosinemia Type II (TYR-II)
Enzyme or other abnormality MIM # / Enzyme Commission #  Elevated tyrosine  Abnormal Newborn Screening Metabolite(s) LOINC Number(s)  Elevated tyrosine S35571-9 Normal succinylacetone S3231-7  Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests  Recommended additional testing to consider at time of initial consultation  Elevated tyrosine (PAA) Elevated tyrosine (PAA) Elevated tyrosine (UOA) Normal succinylacetone Liver function tests  Abnormal Metabolites Expected  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Scheet  American College of Medical Genetics Algorithm  Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel  Secondary Target  Tyrosine elevated, SUAC normal.pdf	MIM #	276600
Abnormal Newborn Screening Metabolite(s)   Elevated tyrosine   3231-7   Plasma amino acids (PAA)   Urine organic acids (UOA) including succinylacetone   Liver function tests   Alpha fetoprotein   Elevated tyrosine (PAA)   Elevated tyrosine (PAA)   Elevated 4-OH-phenylpyruvate, 4-	SNOMED Code / ICD-10-CM Code	4887000 / E70.21
Elevated tyrosine   35571-9   Normal succinylacetone   53231-7	Enzyme or other abnormality	Tyrosine aminotransferase
Abnormal Newborn Screening Metabolite(s)  LOINC Number(s)  S35231-7  Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests  Alpha fetoprotein  Alpha fetoprotein  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal liver function tests expected  Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  American College of Medical Genetics ACT Sheet  Normal succinylacetone  Liver function tests Alpha fetoprotein  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268487%5BDISCUI  %5D&condition=C0268487&compare labs=1  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated; SUAC normal.pdf  Recommended Uniform Screening Panel	MIM # / Enzyme Commission #	613018 / 2.6.1.5
Normal succinylacetone   53231-7     Plasma amino acids (PAA)   Urine organic acids (UOA) including succinylacetone   Liver function tests     Recommended additional testing to consider at time of initial consultation     Abnormal Metabolites Expected   Elevated tyrosine (PAA)   Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA)   Normal succinylacetone (UOA)   Nor		Elevated tyrosine
Initial Diagnostics at Referral Center  Recommended additional testing to consider at time of initial consultation  Elevated tyrosine (PAA) Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA)	Abnormal Newborn Screening Metabolite(s)	35571-9
Plasma amino acids (PAA)     Urine organic acids (UOA) including succinylacetone     Liver function tests     Alpha fetoprotein     Elevated tyrosine (PAA)     Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA)     Normal succinylacetone (UOA)     Normal liver function tests expected     Persistence of tyrosine elevation, with negative succinylacetone     Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes     Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III);     Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn     Specific Testing Laboratories as listed in the Genetic Testing Registry     GeneReviews     American College of Medical Genetics ACT     Sheet     American College of Medical Genetics Algorithm     Recommended Uniform Screening Panel     Plasma amino acids (PAA)     Urine organic acids (UOA) including succinylacetone     Liver function tests     Alpha fetoprotein     Alpha fetoprotein     Alpha fetoprotein     Alpha fetoprotein (PAA)     Elevated tyrosine (PAA)     Pryosine elevated, succinylacetone normal:     Tyrosine elevated, succinylacetone normal:     Tyrosine elevated, SUAC normal.pdf	LOINC Number(s)	Normal succinylacetone
Initial Diagnostics at Referral Center  Recommended additional testing to consider at time of initial consultation  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal Succinylacetone (UOA) Normal liver function tests expected  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  Recommended Uniform Screening Panel  Urine organic acids (UOA) Alpha fetoprotein  Elevated tyrosine (PAA)  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal succinylacetone (UOA) Normal superior (PAA)  Elevated tyrosine (PAA)  Flevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylaceton (UOA) Normal succinylacetone (UOA) Normal succinylacetone (UOA) Normal succinylacetone, 12 (PAB)  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel	· ,	•
Liver function tests		Plasma amino acids (PAA)
Liver function tests	Initial Diagnostics at Referral Center	Urine organic acids (UOA) including succinylacetone
Abnormal Metabolites Expected  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Recommended Uniform Screening Panel  Applia recoprocein (PAA)  Elevated 4-OH-phenylpyruvate, 4-OH-phenylpicate, 4-tyramine, N-acetyltyrosine (UOA)  Normal succinylacetone (UOA)  Tyrosine elevated, SulAC normal pdf  Secondary Target		
Abnormal Metabolites Expected  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Recommended Uniform Screening Panel  Applia retoprotein  Elevated 4-OH-phenylpyruvate, 4-OH-phenylpactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Norma	Recommended additional testing to consider	
Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Genetic Testing Registry  Genetic Testing Registry  Mone  American College of Medical Genetics Algorithm  Elevated 4-OH-phenylpyruvate, 4-OH-phenylpacted, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268487%5BDISCUI %5D&condition=C0268487&compare labs=1  Www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tylgorithms/Visio- Tyrosine elevated, SUAC normal.pdf  Secondary Target		Alpha fetoprotein
Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel	V	Elevated tyrosine (PAA)
tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated, SUAC normal.pdf  Secondary Target  Secondary Target		, , , ,
Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  None  American College of Medical Genetics ACT Sheet  None  Mean College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine elevated, SUAC normal.pdf  Secondary Target  Secondary Target		
Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics Algorithm  Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268487%5BDISCUI %5D&condition=C0268487&compare labs=1  Www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC_normal.pdf  Recommended Uniform Screening Panel	Abnormal Metabolites Expected	
Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics  Algorithm  Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the newborn (Secondario College of Secondario College of Secondario College of Secondario College of Secondario College of Medical Genetics ACT (Secondario College of Medical Genetics Algorithms)  Tyrosine elevated, SUAC normal.pdf  Secondario Target		
If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics  Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC normal.pdf  Secondary Target		1
Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  None  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel  Secondary Target	If initial testing is negative has the disorder	• • • • • • • • • • • • • • • • • • • •
Diagnostic Confirmation  Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel  Secondary Target		Yes
Diagnostic Confirmation  Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel  Secondary Target		Persistence of tyrosine elevation, with negative succinvlacetone
newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine elevated, SUAC normal.pdf  Secondary Target	Diagnostic Confirmation	
Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TPR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TPR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TRA II); Total Parenteral Nutrition (TPN), Transient Tyrosine Absorbance III (TRA II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TAR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Type III (TRA II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia Tyros		· · · · · · · · · · · · · · · · · · ·
Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine elevated, SUAC normal.pdf  Secondary Target		
the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, Suac normal.pdf  Recommended Uniform Screening Panel  Secondary Target	Differential Diagnosis	
Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC normal.pdf  Secondary Target	Differential Diagnosis	, , , ,
Genetic Testing Registry       %5D&condition=C0268487&compare labs=1         Specific Testing Laboratories as listed in the Genetic Testing Registry       None         American College of Medical Genetics ACT Sheet       www.acmg.net/StaticContent/ACT/Tyrosine.pdf         American College of Medical Genetics Algorithm       Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine elevated, SUAC normal.pdf         Recommended Uniform Screening Panel       Secondary Target	Specific Testing Laboratories as listed in the	
Specific Testing Laboratories as listed in the Genetic Testing Registry       None         GeneReviews       None         American College of Medical Genetics ACT Sheet       www.acmg.net/StaticContent/ACT/Tyrosine.pdf         American College of Medical Genetics Algorithm       Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf         Recommended Uniform Screening Panel       Secondary Target		• •
Genetic Testing Registry       None         American College of Medical Genetics ACT Sheet       www.acmg.net/StaticContent/ACT/Tyrosine.pdf         American College of Medical Genetics Algorithm       Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf         Recommended Uniform Screening Panel       Secondary Target		/// // // // // // // // // // // // //
GeneReviews       None         American College of Medical Genetics ACT Sheet       www.acmg.net/StaticContent/ACT/Tyrosine.pdf         American College of Medical Genetics Algorithm       Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine elevated, SUAC normal.pdf         Recommended Uniform Screening Panel       Secondary Target		
American College of Medical Genetics ACT Sheet  American College of Medical Genetics American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine_elevated, SUAC_normal.pdf  Recommended Uniform Screening Panel  Secondary Target	, i	
Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine_elevated, SUAC_normal.pdf  Secondary Target	GeneReviews	None
American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel  Secondary Target	American College of Medical Genetics ACT	www.aama.not/StatioContent/ACT/Tyrosina.ndf
American College of Medical Genetics Algorithm  www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel  Secondary Target	Sheet	www.acmg.net/StaticContent/ACT/Tyrosme.pui
Algorithm  Algorithm  Recommended Uniform Screening Panel  Secondary Target		Tyrosine elevated; succinylacetone normal:
Recommended Uniform Screening Panel  Secondary Target  Secondary Target		www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Secondary Larger		
Secondary Larger	Recommended Uniform Screening Panel	
	, , , , , , , , , , , , , , , , , , ,	Secondary Target

### Tyrosinemia Type III (TYR-III); 4-Hydroxyphenylpyruvic Acid Oxidase Deficiency (Amino Acidemia)

Disease (common abbreviation)  MIM # SNOMED Code / ICD-10-CM Code Enzyme or other abnormality  Acid Oxidase Deficiency 276710   415764005   E70.21	(I	Amino Acidemia)
SNOMED Code / ICD-10-CM Code Enzyme or other abnormality 415764005 / E70.21 41-Hydroxyphenylpyruvic acid oxidase 276710 / 1.13.11.27 Elevated tyrosine 35571-9 Normal succinylacetone 53231-7 Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests Alpha fetoprotein Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone Liver function tests Alpha fetoprotein Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal succinylacetone Liver function tests Alpha fetoprotein Elevated tyrosine of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn Specific Testing Laboratories as listed in the Genetic Testing Laboratories as listed in the Genetic Testing Registry GeneReviews None  None  Merican College of Medical Genetics ACT Sheet Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf Tyrosine elevated; SUAC_normal.pdf	Disease (common abbreviation)	Tyrosinemia Type III (TYR-III); 4-Hydroxyphenylpyruvic
### Abnormal Newborn Screening Metabolite(s)  Abnormal Newborn Screening Metabolite(s)  Abnormal Newborn Screening Metabolite(s)  LOINC Number(s)  Blevated tyrosine  35571-9  Plasma amino acids (PAA)  Urine organic acids (UOA) including succinylacetone  Liver function tests  Alpha fetoprotein  Elevated tyrosine (PAA)  Blevated tyrosine (PAA)  Urine organic acids (UOA) including succinylacetone  Liver function tests  Alpha fetoprotein  Elevated tyrosine (PAA)  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA)  Normal succinylacetone (UOA)  Normal sulver function tests expected  Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone  Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II);  Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  Recommended Uniform Screening Panel  Recommended Uniform Screening Panel	MIM#	Acid Oxidase Deficiency
#Hydroxyphenylpyruvic acid oxidase 276710 / 1.13.11.27  #Belevated tyrosine 35571-9  Normal succinylacetone 53231-7    Plasma amino acids (PAA)   Urine organic acids (UOA) including succinylacetone   Liver function tests	SNOMED Code / ICD-10-CM Code	276710
## Abnormal Newborn Screening Metabolite(s) ## Abnormal Screening Metabolites at Referral Center  ## Plasma amino acids (PAA) ## Urine organic acids (UOA) including succinylacetone ## Liver function tests ## Alpha fetoprotein ## Alpha fetoprotein ## Elevated tyrosine (PAA) ## Elevated tyrosine (UOA) ## Normal succinylacetone normal: ## Noresine elevated, succinylacetone normal: ## Noresine elevated, succinylacetone normal: ## Noresine elevated, SuAC_normal.pdf ## Noresine elevated, SuAC_normal.pdf ## Noresine elevated, SuAC_normal.pdf ## Noresine elevated, SuAC_normal.pdf	Enzyme or other abnormality	415764005 / E70.21
## Abnormal Newborn Screening Metabolite(s) ## Abnormal Succinylacetone ## S2331-7 ## Plasma amino acids (PAA) ## Urine organic acids (UOA) including succinylacetone ## Liver function tests ## Alpha fetoprotein ## Elevated tyrosine (PAA) ## Elevated 4-OH-phenylpyruvate, 4-OH-phenylplactate, 4- ## Uryamine, N-acetyltyrosine (UOA) ## Normal succinylacetone (UOA) ## Normal succinylacetone (UOA) ## Normal liver function tests expected ## Normal succinylacetone (UOA) *# Normal succinylacetone normal: ## Waw.acmg.net/StaticContent/ACT/Tyrosine.pdf ## Noresine.elevated, SUAC_normal.pdf ## Noresine.elevated, SUAC_normal.pdf ## Normal succinylacetone (UOA) ## Normal succinylacetone (UOA) *# Normal succinylacetone (UOA		4-Hydroxyphenylpyruvic acid oxidase
Abnormal Newborn Screening Metabolite(s)  LOINC Number(s)  S3531-7  Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests  Alpha fetoprotein  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal liver function tests expected  Normal liver function tests expected  Abnormal Metabolites Expected  Fersistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Mormal succinylacetone  Alpha fetoprotein  Alpha fetoprote	MIM # / Enzyme Commission #	
Normal succinylacetone   S3231-7     Plasma amino acids (PAA)   Urine organic acids (UOA) including succinylacetone   Liver function tests     Recommended additional testing to consider at time of initial consultation     Alpha fetoprotein     Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA)   Normal succinylacetone (UOA)   Normal s		Elevated tyrosine
LOINC Number(s)  Normal succinylacetone 53231-7  Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests  Recommended additional testing to consider at time of initial consultation  Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Registry  None  American College of Medical Genetics Algorithm  Normal succinylacetone Liver function tests Alpha fetoprotein  Elevated tyrosine (PAA)  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA)  Normal succinylacetone  Alpha fetoprotein  Elevated tyrosine (PAA)  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA)  Normal succinylacetone (UOA)  Normal succinylacetone  (UOA)  Normal succinylacetone  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA)  Normal succinylacetone  Yes  Pristing Laboratories as listed in the Specific Testing Laboratories as listed in the Genetic Testing Registry  None  Www.achi.nlm.nih.gov/gtr/tests/?term=C0268623%c5BDISCUI %5D&condition=C0268623&compare labs=1  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC_normal.pdf	Abnormal Newborn Screening Metabolite(s)	35571-9
S3231-7   Plasma amino acids (PAA)   Urine organic acids (UOA) including succinylacetone   Liver function tests		Normal succinylacetone
Initial Diagnostics at Referral Center  Recommended additional testing to consider at time of initial consultation  Alpha fetoprotein  Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal liver function tests expected  Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  Mecommended Uniform Screening Panel  Verse  Liver function tests Alpha fetoprotein  Elevated tyrosine (PAA)  Elevated tyrosine elevated, succinylacetone normal:  www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268623%5BDISCUI  %5D&condition=C0268623&compare labs=1  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine elevated, SUAC_normal.pdf	, <i>,</i>	
Initial Diagnostics at Referral Center  Recommended additional testing to consider at time of initial consultation  Alpha fetoprotein  Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal liver function tests expected  Normal succinylacetone (UOA) Normal liver function tests expected  Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  Mecommended Uniform Screening Panel  Secondary Target  Urine organic acids (UOA) including succinylacetone Liver function tests  Alpha fetoprotein  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, 0-ACH-phenyllactate, 4-tyramine, 0-ACH-phenyllactate, 4-OH-phenyllactate, 4-OH-phenyllacterone levated, 5UAC_normal.pdf  Recommended Uniform Screening Panel		Plasma amino acids (PAA)
Liver function tests  Recommended additional testing to consider at time of initial consultation  Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Mone  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; SUAC_normal.pdf  Recommended Uniform Screening Panel  Secondary Target	Initial Diagnostics at Referral Center	
Recommended additional testing to consider at time of initial consultation  Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Mone  Merican College of Medical Genetics ACT Sheet  Merican College of Medical Genetics Algorithm  Alpha fetoprotein Elevated 4-OH-phenylpyruvate, 4-OH-phenylpather, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal succinylacetone (UOA) Normal succinylacetone nermal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC normal.pdf  Secondary Target		
Abnormal Metabolites Expected  Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal succinylacetone (UOA) Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Mone  Merican College of Medical Genetics Algorithm  Recommended Uniform Screening Panel  Applia retoprotein Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenylpacetone (UOA) Normal succinylacetone (UOA) Normal succinylacetone (UOA) Normal succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Persistence of tyrosine elevated, succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC_normal.pdf  Secondary Target	Recommended additional testing to consider	
Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Genetic Testing Registry  Genetic Testing Registry  None  Maerican College of Medical Genetics Algorithm  Elevated 4-OH-phenylpyruvate, 4-OH-phenylpacted, 4-OH-phenylpacted, 4-OH-phenylpyruvate, 4-OH-phenylpyruvate, 4-OH-phenylpyruvate, 4-OH-phenylpacted, 4-OH-phenylpyruvate, 4-OH-phenylpyrusine (UOA) Normal liver function tests expected Normal succinylacetone (UOA)  Normal liver function tests expected Normal succinylacetone pyroid)  Elevated, 5-OH-phenylpyruvate, 4-OH-phenylpyruvate, 4-OH-phenylpyruvate, 4-OH-phenylpyrusie elevated, 5-OH-phenylogs  Www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Secondary Target		Alpha fetoprotein
Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4- tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal super function tests expected Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC_normal.pdf  Secondary Target	· · · · · · · · · · · · · · · · · · ·	Elevated tyrosine (PAA)
tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics Algorithm  tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (IOA) Nore  Tyrosine elevated, SuAC normal.pdf		
Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC_normal.pdf  Secondary Target		
Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Normal liver function (after neonatal period)  Yes  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268623%5BDISCUI %5D&condition=C0268623&compare labs=1  Specific Testing Laboratories as listed in the GeneReviews  None  Tyrosine elevated; Succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; Succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine_elevated, SUAC_normal.pdf	Abnormal Metabolites Expected	
Normal alpha fetoprotein (after neonatal period)  If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf  Secondary Target		
If initial testing is negative has the disorder been ruled out?  Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics  Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf  Secondary Target		<u>-</u>
Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Registry  None  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC_normal.pdf  Secondary Target	If initial testing is negative has the disorder	
Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  Medical Genetics  None  Www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC_normal.pdf  Secondary Target	· ·	Yes
Diagnostic Confirmation  Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC normal.pdf  Recommended Uniform Screening Panel  Secondary Target		Persistence of tyrosine elevation, with negative succinvlacetone
newborn (TTN) and nongenetic causes  Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics  Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine elevated, SUAC_normal.pdf  Secondary Target	Diagnostic Confirmation	
Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics  Algorithm  Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  www.acmg.neline.nih.gov/gtr/tests/?term=C0268623%5BDISCUI %5D&condition=C0268623&compare labs=1  None  Www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf  Recommended Uniform Screening Panel  Secondary Target	Diagnostic Confirmation	l
Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics  Algorithm  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf  Secondary Target		· · · · · ·
Newborn   Specific Testing Laboratories as listed in the Genetic Testing Registry   Www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268623%5BDISCUI %5D&condition=C0268623&compare labs=1   Specific Testing Laboratories as listed in the Genetic Testing Registry   None   None   None   Www.acmg.net/StaticContent/ACT/Tyrosine.pdf   Tyrosine elevated; succinylacetone normal:   www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf   Secondary Target	Differential Diagnosis	
Specific Testing Laboratories as listed in the Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Laboratories as listed in the Genetic Testing Registry  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine_elevated, SUAC_normal.pdf  Secondary Target	Differential Diagnosis	, /·
Genetic Testing Registry  Specific Testing Laboratories as listed in the Genetic Testing Registry  GeneReviews  None  American College of Medical Genetics ACT Sheet  American College of Medical Genetics ACT Sheet  Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated, SUAC_normal.pdf  Recommended Uniform Screening Panel  Secondary Target	Specific Testing Laboratories as listed in the	
Specific Testing Laboratories as listed in the Genetic Testing Registry       Specific Testing Registry         GeneReviews       None         American College of Medical Genetics ACT Sheet       www.acmg.net/StaticContent/ACT/Tyrosine.pdf         Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf         Recommended Uniform Screening Panel       Secondary Target		
Genetic Testing Registry       None         American College of Medical Genetics ACT Sheet       www.acmg.net/StaticContent/ACT/Tyrosine.pdf         American College of Medical Genetics Algorithm       Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf         Recommended Uniform Screening Panel       Secondary Target		703D&COHUHIOH=C0208023&COHIPAFE_IAD8=1
GeneReviews       None         American College of Medical Genetics ACT Sheet       www.acmg.net/StaticContent/ACT/Tyrosine.pdf         American College of Medical Genetics Algorithm       Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated, SUAC_normal.pdf         Recommended Uniform Screening Panel       Secondary Target		
American College of Medical Genetics ACT Sheet  Www.acmg.net/StaticContent/ACT/Tyrosine.pdf  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine_elevated,_SUAC_normal.pdf  Recommended Uniform Screening Panel  Secondary Target	Geneue Testing Registry	
Sheet  American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio-  Tyrosine_elevated,_SUAC_normal.pdf  Recommended Uniform Screening Panel  Secondary Target	GeneReviews	None
American College of Medical Genetics Algorithm  Tyrosine elevated; succinylacetone normal:  www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine_elevated,_SUAC_normal.pdf  Secondary Target	American College of Medical Genetics ACT	www.aama.not/StatiaContant/ACT/Tyrosina.ndf
American College of Medical Genetics Algorithm  www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine_elevated,_SUAC_normal.pdf  Recommended Uniform Screening Panel  Secondary Target	~ · ·	www.acing.net/StaticContent/AC1/Tyrosine.pdf
Algorithm	American College of Madiana Counting	Tyrosine elevated; succinylacetone normal:
Algorithm Tyrosine_elevated, SUAC_normal.pdf  Recommended Uniform Screening Panel Secondary Target	e v	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Recommended Uniform Screening Panel Secondary Target	Algorithm	
Secondary Larger	Recommended Uniform Screening Panel	
	· ·	Secondary Target

### Carnitine Palmitoyl Transferase Type Ia Deficiency (CPT-Ia) (Fatty Acid Oxidation Disorder)

(ratty A	cid Oxidation Disorder)
Disease (common abbreviation)	Carnitine Palmitoyl Transferase Type Ia Deficiency (CPT-Ia)
MIM#	255120
SNOMED Code / ICD-10-CM Code	238001003 / E71.314
Enzyme or other abnormality	Carnitine palmitoyl transferase Ia
MIM # / Enzyme Commission #	600528 / 2.3.1.21
	Elevated C0
Abnormal Newborn Screening Metabolite(s)	38481-8
LOINC Number(s)	Elevated C0/(C16+C18) ratio*
	53235-8
	Carnitine, total and free in blood spot (<1 wk)
Initial Diggraphing at Reformal Conton	Carnitine, total and free in plasma (>1 wk)
Initial Diagnostics at Referral Center	Plasma acylcarnitine profile
	Blood spot Acylcarnitine profile
Recommended additional testing to consider	Liver function tests
at time of initial consultation	Blood glucose
	Normal/elevated carnitine
	Decreased C16 and C18
Abnownal Motabalitas Europetad	Elevated C0/(C16+C18) (blood spot < 1 wk)
Abnormal Metabolites Expected	Low Esterified/Free Carnitine (plasma)
	Normal liver function tests expected
	Glucose levels depend on fed status of patient
If initial testing is negative has the disorder	Yes
been ruled out?	
	* If initial C0/(C16+C18) ratio >100 or if expected abnormal
	metabolites are seen (Blood spot ratios valid in infants less
Diagnostic Confirmation	than one week of age, older patients will need additional
	diagnostic confirmation)
	Mutation analysis (CPT1A mutation analysis)
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342789%5BDISCUI
Genetic Testing Registry	%5D&condition=C0342789&compare_labs=1
Specific Testing Laboratories as listed in the	
Genetic Testing Registry	
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1527/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C0_C16-C18.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	<u>C0.vsd;</u> <u>C0.vsd;</u> <u>C16-C18.pdf</u>
Recommended Uniform Screening Panel (RUSP)	Secondary Target

### Carnitine Palmitoyl Transferase Type II Deficiency (CPT-II) (Fatty Acid Oxidation Disorder)

Disease (common abbreviation)	Carnitine Palmitoyl Transferase Type II Deficiency (CPT-II)
MIM#	600649 (infantile), 608836 (lethal neonatal)
SNOMED Code / ICD-10-CM Code	238002005 / E71.314
Enzyme or other abnormality	Carnitine palmitoyl transferase II
MIM # / Enzyme Commission #	600650 / 2.3.1.21
	Elevated C16
Abnormal Newborn Screening Metabolite(s)	53199-6
LOINC Number(s)	Elevated C18:1
	53202-8
Initial Diagnostics at Referral Center	Carnitine, total and free and acylcarnitine profile in plasma
Recommended additional testing to consider	Creatinine phosphokinase (CPK)
at time of initial consultation	Blood glucose
	Normal/Decreased free carnitine Elevated C16, C18:1
Abnormal Metabolites Expected	CPK may be elevated in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder	Yes
been ruled out?	ies
	Enzyme assay in fibroblasts and/or mutation analysis with
Diagnostic Confirmation	detection of two known or likely pathological mutations in
	trans
Differential Diagnosis	Carnitine-Acylcarnitine Translocase Deficiency (CACT)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342790%5BDISCUI
Genetic Testing Registry	%5D&condition=C0342790&compare_labs=1
Specific Testing Laboratories as listed in the	
Genetic Testing Registry	
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1253/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C16_and-or_C18-1.pdf
Sheet	www.acmg.net/StaticContent/AC1/C10_and-oi_C18-1.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C16_and-
Algorithm	or_C18.pdf
Recommended Uniform Screening Panel	Secondary Target
(RUSP)	Secondary Target

### Carnitine-Acylcarnitine Translocase Deficiency (CACT) (Fatty Acid Oxidation Disorder)

\	Cid Oxidation Disorder)
Disease (common abbreviation)	Carnitine-Acylcarnitine Translocase Deficiency (CACT)
MIM #	255110
SNOMED Code / ICD-10-CM Code	238003000 / E71.318
Enzyme or other abnormality	Carnitine-acylcarnitine translocase
MIM # / Enzyme Commission #	212138 / 2.3.1.21
	Elevated C16
Abnormal Newborn Screening Metabolite(s)	53199-6
LOINC Number(s)	Elevated C18:1
	53202-8
Initial Diagnostics at Referral Contan	Carnitine, total and free in plasma
Initial Diagnostics at Referral Center	Acylcarnitine profile in plasma
Recommended additional testing to consider	Creatinine phosphokinase (CPK)
at time of initial consultation	Blood glucose
	Decreased free carnitine
Almania Matabalitas Empartad	Elevated C16, C18:1
Abnormal Metabolites Expected	CPK may be elevated in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder	V
been ruled out?	Yes
	Mutation analysis with detection of two known or likely
Diagnostic Confirmation	pathological mutations in trans
Differential Diagnosis	Carnitine Palmitoyl Transferase Type II Deficiency (CPT II)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342791%5BDISCUI
Genetic Testing Registry	%5D&condition=C0342791&compare_labs=1
Specific Testing Laboratories as listed in the	%5D&condition=C0342/91&compare_labs=1
1 0	
Genetic Testing Registry	
GeneReviews	None
American College of Medical Genetics ACT	www.aama.nat/StatioContent/ACT/C16 and an C10 1 alf
Sheet	www.acmg.net/StaticContent/ACT/C16_and-or_C18-1.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C16_and-
Algorithm	or_C18.pdf
Recommended Uniform Screening Panel	Sacandary Target
(RUSP)	Secondary Target
	·

### Carnitine Uptake Defect (CUD); Primary Carnitine Deficiency (Fatty Acid Oxidation Disorder)

\ \	Cid Oxidation Disorder
Disease (common abbreviation)	Carnitine Uptake Defect (CUD); Primary Carnitine Deficiency
MIM#	212140
SNOMED Code / ICD-10-CM Code	21764004 / E71.41
Enzyme or other abnormality	Plasma membrane carnitine transporter
MIM # / Enzyme Commission #	603377 / None
	Decreased C0
Abnormal Newborn Screening Metabolite(s)	38481-8
LOINC Number(s)	Decreased SUM (Acylcarnitines)
	None
	Plasma Carnitine, total and free
Initial Diagnostics at Referral Center	Acylcarnitine profile
o v	Urine Carnitine, total and free
Recommended additional testing to consider	Creatinine phosphokinase (CPK)
at time of initial consultation	Blood glucose
at time of thittat consultation	
	Decreased carnitine, total and free
	Decreased acylcarnitines (long-chain)
Abnormal Metabolites Expected	Elevated total and free urine carnitine
	Reduced carnitine renal reabsorptiom
	CPK can be elevated in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder been ruled out?	Yes (provided no carnitine supplementation)
	Enzyme assay (OCTN2) in fibroblasts and/or mutation analysis
Diagnostic Confirmation	if functional assay unclear
Diagnostic Confirmation	Consider maternal testing
	Consider other non-genetic causes of carnitine deficiency –
Differential Diagnosis	
Differential Diagnosis	
Specific Testing Laboratories as listed in the	
1 0	
<u>U_U_I</u>	70 5D&CONGHON=CU5421 88&COMPARE_IADS=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK84551/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C0.ndf
Sheet	www.acmg.net/StaticContent/AC1/Co.put
American College of Medical Genetics	www.comg.not/StatioContent/ACT/Alcouithme/Visio.CO.rdf
Algorithm	www.acing.net/StaticContent/ACT/Algorithms/V1810-C0.pdf
	Cara Daniel
· · · · · · · · · · · · · · · · · · ·	Core Panel
Sheet American College of Medical Genetics	nutritional, renal insufficiency, other primary IEMs and maternal CUD or IEMs  www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342788%5BDISCUI %5D&condition=C0342788&compare_labs=1  www.ncbi.nlm.nih.gov/books/NBK84551/  www.acmg.net/StaticContent/ACT/C0.pdf  www.acmg.net/StaticContent/ACT/Algorithms/Visio-C0.pdf  Core Panel

### 2,4-Dienoyl-CoA Reductase Deficiency (2,4Di) (Fatty Acid Oxidation Disorder)

	on on one of the original of t
Disease (common abbreviation)	2,4-Dienoyl-CoA Reductase Deficiency (2,4Di)
MIM #	222745
SNOMED Code / ICD-10-CM Code	None / None
Enzyme or other abnormality	2,4-Dienoly-CoA reductase
MIM # / Enzyme Commission #	222745 / 1.3.1.34
Abnormal Newborn Screening Metabolite(s)	Elevated C10:2
LOINC Number(s)	53180-64
Initial Diagnostics at Pefewal Center	Acylcarnitine profile
Initial Diagnostics at Referral Center	Plasma Carnitine, total and free
Recommended additional testing to consider	Urine acylcarnintine profile
at time of initial consultation	Plasma amino acids
	Elevation 2-trans,4-cis-C10:2 in plasma and urine
Abnormal Metabolites Expected	Normal/low plasma carnitine levels
	Normal/elevated lysine
If initial testing is negative has the disorder been ruled out?	Unknown
Diagnostic Confirmation	No specific recommendations
Differential Diagnosis	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=dienoyl-coareductase&condition=CN037048&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT Sheet	No ACT sheet
American College of Medical Genetics Algorithm	No algorithm
Recommended Uniform Screening Panel (RUSP)	Secondary Target

### Long-chain L3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD) (Fatty Acid Oxidation Disorder)

	I 1 2 II 1 1 CAD 1 1 D.C.
Disease (common abbreviation)	Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency
MIM #	(LCHAD) 609016
SNOMED Code / ICD-10-CM Code	237999008 / E71.310
Enzyme or other abnormality	Long-chain L3-Hydroxyacyl-CoA dehydrogenase
MIM # / Enzyme Commission #	600890 / 1.1.1.211
min n / Enzyme Commission n	Elevated C16OH
Abnormal Newborn Screening Metabolite(s)	50125-4
LOINC Number(s)	Elevated C18:10H
Zen (e number (b)	50113-0
	Acylcarnitine profile
	Urine organic acids
Initial Diagnostics at Referral Center	Mutation analysis, as negative metabolites do not rule out the
	disorder
	Liver function tests
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Creatinine phosphokinase (CPK)
	Plasma Carnitine, total and free
	Elevated C16OH, C18:1OH (acylcarnitines)
	Elevated 3-OH-dicarboxylic acids (C6-C14), saturated and
	unsaturated, (UOA) which are only be seen during episodes of
	metabolic decompensation, with normal or absent ketones
Abnormal Metabolites Expected	Detection of known pathological mutation in trans
	Liver function tests may be abnormal in sick patients
	Blood glucose depends on fed status of patient
	CPK may be elevated in sick patients
	Normal/low plasma carnitine levels
If initial testing is negative has the disorder	Yes
been ruled out?	
	Mutation analysis for combined LCHAD/TFP:
	0 mutation - ruled out (unless consanguineous and as long as
Diagnostic Confirmation	metabolites normal)
2 tagaestie Gergamanen	1 pathological mutation - proceed to enzyme assay or
	functional probe
	2 pathological mutations in trans - diagnosis confirmed
Differential Diagnosis	Trifunctional Protein Deficiency (TFP)
Specific Testing Laboratories as listed in	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342786[DISCU
Genetic Testing Registry	I]&condition=CN074230&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C16-OH.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C16-
Algorithm	<u>OH_+C18-1-OH.pdf</u>
Recommended Uniform Screening Panel	Core Panel
(RUSP)	

#### Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD) (Fatty Acid Oxidation Disorder)

cia Oxidation Disorder)
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
201450
128596003 / E71.311
Medium-chain acyl-CoA dehydrogenase
607008 / 1.3.99.3
Elevated C8
53175-6
Lesser elevation of C6 and C10, C10:1
45211-0, 45197-1, 45198-9
Mutation detection in some states
Acylcarnitine profile and
Urine organic acids and/or urine acylglycines
Blood glucose
Plasma Carnitine, total and free
Elevated C6, C8, C10 (acylcarnitines)
C6 <c8>C10</c8>
Elevated hexanoylglycine and suberylglycine (acylglycines)
Blood glucose depends on fed status of patient
Normal/Low plasma carnitine levels
Elevated dicarboxylic acids, especially suberic acid, with no
excess ketones (UOA)
Yes
Tes
Typical pattern of acylcarnitines is diagnostic - C6 <c8>C10</c8>
Elevated urine hexanoglycine and suberylglycine
Mutation analysis widely available
Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT);
Multiple Acyl-CoA Dehydrogenase Deficiency
(MADD)/(Glutaric Acidemia Type 2) (GA 2)
www.ncbi.nlm.nih.gov/gtr/tests/?term=C0220710%5BDISCUI
%5D&condition=C0220710&compare_labs=1
<u> </u>
www.ncbi.nlm.nih.gov/books/NBK1424/
www.acmg.net/StaticContent/ACT/C8_C6_C10.pdf
www.acmg.net/StaticContent/ACT/Algorithms/Visio-
C8.vsd; C6-C10.pdf
Core Panel

#### Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT) (Fatty Acid Oxidation Disorder)

`	du Oxidation Disorder
Disease (common abbreviation)	Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT)
MIM#	602199
SNOMED Code / ICD-10-CM Code	124265004 / None
, , , , , , , , , , , , , , , , , , ,	Medium-chain ketoacyl-CoA thiolase
•	None; sequence unknown / 2.3.1.16
Abnormal Newborn Screening Metabolite(s)	Elevated C6 and C8
LOINC Number(s)	45211-0, 53175-6
Initial Diagnostics at Referral Center	Acylcarnitine profile
Initial Diagnostics at Referral Center	Urine organic acids
	Blood glucose
Recommended additional testing to consider	Urine ketones
at time of initial consultation	Plasma Carnitine, total and free
ai time of initial consultation	Urine acylglycines
	Creatinine phosphokinase (CPK)
	Elevated C6 and C8
	Elevated ketones bodies on urine organic analysis
	Blood glucose depends on fed state of patient
Abnormal Metabolites Expected	Elevated urine ketones
	Normal plasma carnitine levels
	Normal acylglycine profile
	CPK may be elevated in sick patients
If initial testing is negative has the disorder	Unknown
been ruled out?	Chanown
Diagnostic Confirmation	No specific recommendations
	Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD);
Differential Diagnosis	Multiple Acyl-CoA Dehydrogenase Deficiency (MADD)
	(Glutaric Acidemia Type 2) (GA 2)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1865781%5BDISCUI
Genetic Testing Registry	%5D&condition=C1865781&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	No ACT Sheet
Sheet	INU ACT SHEEL
American College of Medical Genetics	No Algorithm
Algorithm	No Algorithm
Recommended Uniform Screening Panel	Secondary Target
(RUSP)	Scondary Target

#### Multiple Acyl-CoA Dehydrogenase Deficiency (MADD); Glutaric Acidemia Type II (GA-II) (Fatty Acid Oxidation Disorder)

MARIA LO A DA LA LA DESTA (MADD)
Multiple Acyl-CoA Dehydrogenase Deficiency (MADD);
Glutaric Acidemia Type II (GA-II)
231680
22886006 / E71.313
Electron Transfer Flavoprotein (alpha, beta subunit)
608053, 130410, 231675 / 1.5.5.1
Elevated C4, C5, C6, C8, C10
53166-5, 45216-9, 45211-0, 53175-6, 45197-1
Acylcarnitine profile
Urine organic acids
Urine acylglycines
Blood glucose
Creatinine phosphokinase (CPK)
Liver function tests
Elevated C4, C5, C6, C8, C10 and long-chain acylcarnitines
Elevated lactate, 2-OH-glutarate, ethylmalonic acid and adipic
acids (UOA)
Elevated isovaleryl-, hexanoyl-, suberylglycine (acylglycines)
Blood glucose depends on fed status of patient
CPK may be elevated in sick patients
Liver function tests may be abnormal in sick patients
Yes
Abnormal metabolite pattern is diagnostic
If not found, need
1) Mutation analysis with two known or likely pathological
mutations in trans, or
2) Enzyme/functional assay
'Grey Zone' can remain, could still be affected, but consider
maternal disorder, mitochondrial disorder, riboflavin
deficiency
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD);
Medium-chain Ketoacyl-CoA Thiolase Deficiency
(MCKAT), Mitochondrial Disorder, Riboflavin Deficiency,
Maternal Disorder
www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268596%5BDISCUI
%5D&condition=C0268596&compare_labs=1
None
www.acmg.net/StaticContent/ACT/C4_C5.pdf
www.acmg.net/StaticContent/ACT/Algorithms/Visio-
C4 C5 + other AC.pdf
Secondary Target

### Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD) (Fatty Acid Oxidation Disorder)

	or o
Disease (common abbreviation)	Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD)
MIM #	201470
SNOMED Code / ICD-10-CM Code	124166007 / E71.312
Enzyme or other abnormality	Short-chain acyl-CoA dehydrogenase
MIM # / Enzyme Commission #	606885 / 1.3.99.2
Abnormal Newborn Screening Metabolite(s)	Elevated C4
LOINC Number(s)	53166-5
	Urine organic acids (UOA)
Initial Diggraphing at Reformal Conton	Plasma acylcarnitine profile
Initial Diagnostics at Referral Center	Urine acylglycine levels
	Urine C4 acylcarnitines
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Plasma Carnitine, total and free
·	Elevated ethylmalonic acid (UOA)
	Elevated butyrylglycine (urine acylglycines)
Abnormal Metabolites Expected	+/- Elevated urine C4 levels
*	Blood glucose depends on fed status of patient
	Normal/low carnitine levels
If initial testing is negative has the disorder	37
been ruled out?	Yes
	Mutation analysis with 2 known or likely pathological
Diagnostic Confirmation	mutations in trans
	Ethylmalonic Encephalopathy (EMA); Isobutyryl-CoA
Differential Diagnosis	Dehydrogenase Deficiency (IBCD); presence of SCAD
Dijjerenitai Diagnosis	polymorphisms
Specific Testing Laboratories as listed in the	
Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=short-chain+acyl+coa
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK63582/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C4.pdf
Sheet	www.acmg.nevolaticContent/AC1/C4.ptil
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4.pdf
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/v1810-C4.pdf
Recommended Uniform Screening Panel	Secondary Target
(RUSP)	Secondary Target

## Medium/Short-chain L-3-Hydroxyacyl-CoA Dehydrogenase Deficiency (M/SCHAD); 3-@Hydroxyacyl-Co-A Dehydrogenase Deficiency (HADH) (Fatty Acid Oxidation Disorder)

Disease (common abbreviation)	Medium/Short-chain L-3-Hydroxyacyl-CoA Dehydrogenase
	Deficiency (M/SCHAD); 3-@Hydroxyacyl-Co-A
	Dehydrogenase Deficiency (HADH)
MIM #	231530
SNOMED Code / ICD-10-CM Code	237998000 / None
Enzyme or other abnormality	Short-chain L-3-hydroxyacyl-CoA dehydrogenase
MIM # / Enzyme Commission #	601609 / 1.1.1.35
Abnormal Newborn Screening Metabolite(s)	Elevated C4OH
LOINC Number(s)	50102-3
	Plasma acylcarnitine profile
	Urine organic acids
Initial Diagnostics at Referral Center	Plasma 3-OH-fatty acids
	Glucose
	Insulin
Recommended additional testing to consider at time of initial consultation	Free fatty acids
	Elevated C4OH
Abnormal Metabolites Expected	Elevated/normal ketone bodies on urine organic analysis
Nonormai Meidobilles Expected	Blood glucose depends on fed status of patient
	Severe hyperinsulinemic hypoglycemia in one case
If initial testing is negative has the disorder been ruled out?	Unknown
D' C C C	Enzyme analysis in blood leukocytes
Diagnostic Confirmation	Mutation analysis
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=Hydroxyacyl-CoA
* *	Dehydrogenase Deficiency
Genetic Testing Registry	&condition=C1291230&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C4-OH.pdf
	yyyyy aama not/StatiaContant/ACT/Algorithma/Visia CA
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4-OH.pdf
Algorithm  Pagaman ded Uniform Someoning Band	O11.pui
Recommended Uniform Screening Panel (RUSP)	Secondary Target

#### Trifunctional Protein Deficiency (TFP) (Fatty Acid Oxidation Disorder)

Disease (common abbreviation)  Trifunctional Protein Deficiency (TFP)		
Trifunctional Protein Deficiency (TFP)		
609015		
237999008 / E88.39		
Trifunctional protein (alpha, beta subunit)		
600890, 143450 / 1.1.1.211		
Elevated C16OH		
50125-4		
Elevated C18:1OH		
50113-0		
Acylcarnitine profile		
Urine organic acids		
Mutation analysis, as negative metabolites do not rule out the		
disorder		
Liver function tests		
Blood glucose		
Creatinine phosphokinase (CPK)		
Plasma Carnitine, total and free		
Elevated C16OH, C18:1OH (acylcarnitines)		
Elevated 3-OH-dicarboxylic acids (C6-C14), saturated and		
unsaturated (UOA) which are only be seen during episodes of		
metabolic decompensation, with normal or absent ketones		
Detection of known pathological mutations in trans		
Liver function tests may be abnormal in sick patients		
Blood glucose depends on fed status of patient		
CPK may be elevated in sick patients  Normal/low carnitine levels		
Normal/low carmine levels		
Yes		
Mutation analysis for combined LCHAD/TFP:		
0 mutation – disease unlikely (unless consanguineous and as		
long as metabolites normal)		
1 known or likely pathological mutation - proceed to enzyme		
assay or functional (probe) study		
2 known or likely pathological mutations in trans – diagnosis		
confirmed		
Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency		
(LCHAD)		
www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342786%5BDISCUI		
%5D&condition=C0342786&compare_labs=1		
None		
www.acmg.net/StaticContent/ACT/C16-OH.pdf		
www.acmg.net/StaticContent/ACT/Algorithms/Visio-C16-		
OH_+C18-1-OH.pdf		
Core Panel		
CORE FAIRE		

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

` '	ciu Oxidation Disorder)
Disease (common abbreviation)	Very Long-chain Acyl-CoA Dehydrogenase Deficiency
MIM //	(VLCAD)
MIM#	201475
SNOMED Code / ICD-10-CM Code	237997005 / E71.310
Enzyme or other abnormality  MIM # / Enzyma Commission #	Very long-chain acyl-CoA dehydrogenase 609575 / 1.3.99.13
MIM # / Enzyme Commission #	Elevated C14
Abnormal Newborn Screening Metabolite(s)	53192-1
LOINC Number(s)	Elevated C14:1
Lonve (vanioer(s)	53191-3
	Plasma acylcarnitine profile
Initial Diagnostics at Referral Center	Mutation analysis, as negative metabolites do not rule out the
muiai Diagnosiies ai Rejerrai Cemer	disorder
	Blood glucose Plasma Carnitine, total and free
Recommended additional testing to consider	Creatinine phosphokinase (CPK)
at time of initial consultation	Urine organic acids
	Liver function tests
	Elevated C14, C14:1
	Detection of known pathological mutations in trans
	Blood glucose depends on fed status of patient
Abnormal Metabolites Expected	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
If initial testing is negative has the disorder been ruled out?	No
	Mutation analysis:
	0 mutation disease unlikely (unless consanguineous, and as
Diagnostic Confirmation	long as metabolites are normal)
Diagnosiie Congilmanon	1 mutation - proceed to enzyme assay or functional probe
	2 known or likely pathological mutations in trans confirms
	diagnosis
	Carnitine Palmitoyl Transferase Type II Deficiency (CPT II),
Differential Diagnosis	Carnitine-Acylcarnitine Translocase Deficiency (CACT), Multiple Acyl-CoA Dehydrogenase Deficiency (MADD),
	Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency
	(LCHAD)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342784%5BDISCUI
Genetic Testing Registry	%5D&condition=C0342784&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK6816/
American College of Medical Genetics ACT	
Sheet	www.acmg.net/StaticContent/ACT/C14.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C14-
Algorithm	1_DM.pdf

Recommended	Uniform	Screening	Panel
(RUSP)			

Core Panel

### Ethylmalonic Encephalopathy (EMA) (Fatty Acid Oxidation Disorder)

	Ciu Oxidation Disorder)
Disease (common abbreviation)	Ethylmalonic Encephalopathy (EMA)
MIM #	602473
SNOMED Code / ICD-10-CM Code	81308009 / G93.41
Enzyme or other abnormality	ETHE1 protein
MIM # / Enzyme Commission #	608451 / 1.5.5.1
	Elevated C4 and C5
	53166-5/???
Abnormal Newborn Screening Metabolite(s)	Elevated C4/C3 ratio
LOINC Number(s)	53168-1
· /	Elevated C5/C2 ratio
	53239-0
	Urine organic acids (UOA)
	Acylcarnitine profile
Initial Diagnostics at Referral Center	Urine acylglycine levels (UAG)
	(urine C4 acylcarnitines)
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Carnitine, total and free
at time of initial consultation	Elevated ethylmalonic acid, methylsuccinic acid and lactate
	(UOA)
	Elevated C4 in plasma and urine
Abnormal Metabolites Expected	Elevated C4 in plasma and urine Elevated isobutyrylglycine and 2-methylbutyrylglycine (UAG)
	Blood glucose depends on fed status of patient
	Normal/low plasma carnitine levels
If initial testing is negative has the disorder	Normal/low plasma carmine levels
been ruled out?	Yes
been ruiea oui?	Aba amada matah alita mattam with alimi ad mbanatam
Diamondia Canfinandian	Abnormal metabolite pattern with clinical phenotype
Diagnostic Confirmation	Mutation analysis with two known or likely pathological
	mutations in trans (may not be available in US)
Differential Diagnosis	Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD);
2 off continue Deagnosis	Isobutyryl-CoA Dehydrogenase Deficiency (IBCD)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1865349%5BDISCUI
Genetic Testing Registry	%5D&condition=C1865349&compare_labs=1
	•
GeneReviews	None
American College of Medical Genetics ACT	
Sheet	www.acmg.net/StaticContent/ACT/C4.pdf
American College of Medical Genetics	100 1 C 1 1/4 CP/11 12 17 17 1 C1 12
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4.pdf
Recommended Uniform Screening Panel	N. D. I
(RUSP)	Not on Panel
/	I

Isobutyryl-CoA Dehydrogenase Deficiency (IBCD); Isobutyrylglycinuria (IBG) (Organic Acidemia)

	rgame Actucinia)
Disease (common abbreviation)	Isobutyryl-CoA Dehydrogenase Deficiency (IBCD);
	Isobutyrylgylcinuria (IBG)
MIM #	604773
SNOMED Code / ICD-10-CM Code	124136000 / E71.19
Enzyme or other abnormality	Isobutyryl-CoA dehydrogenase
MIM # / Enzyme Commission #	604773 / 1.1.1.157
Abnormal Newborn Screening Metabolite(s)	Elevated C4
LOINC Number(s)	53166-5
	Urine organic acids
Listial Diagraphics at Reformal Conton	Acylcarnitine profile
Initial Diagnostics at Referral Center	Urine acylglycine levels
	Urine C4 acylcarnitines
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Carnitine, total and free
	Elevated C4 in plasma and urine
	Normal ethylmalonic acid
Abnormal Metabolites Expected	Elevated isobutyrylglycine
•	Blood glucose depends on feeding status of patient
	Normal/Low plasma carnitine levels
If initial testing is negative has the disorder	V
been ruled out?	Yes
Diagnostic Confirmation	Abnormal metabolite pattern, and mutation analysis with two
Diagnostic Confirmation	known or likely pathological mutations in trans
Differential Discourse	Ethylmalonic Encephalopathy (EMA); Short-chain Acyl-CoA
Differential Diagnosis	Dehydrogenase Deficiency (SCAD)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1969809%5BDISCUI
Genetic Testing Registry	%5D&condition=C1969809&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C4.pdf
Sheet	
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

### $\label{eq:condition} \begin{tabular}{ll} Methylmalonic Acidemia - Cobalamin A,B Cofactor Deficiency (Cbl A,B); Cobalamin D_1 \\ Cofactor Deficiency (CblD_1) \end{tabular}$

(Organic Acidemia)

(0	rgaint Actuenna)
Disease (common abbreviation)	Methylmalonic Aciduria - Cobalamin A,B Cofactor (Cbl A,B);
Discuse (common aboreviation)	Cobalamin D <sub>1</sub> Cofactor Deficiency (Cbl D <sub>1</sub> )
MIM#	251100 (A), 251110 (B)
SNOMED Code / ICD-10-CM Code	73843004 (A), 82245003 (B) / E71.120
	Cobalamin A,B cofactor deficiency
Enzyme or other abnormality	607481 (A), 607568 (B)
MIM#	Cobalamin D <sub>1</sub> cofactor
/Enzyme Commission #	611935 / 5.4.99.2
	Elevated C3
Abnormal Newborn Screening Metabolite(s)	53160-8
LOINC Number(s)	Elevated C4DC
	45222-7
	Urine organic acids (UOA)
	Plasma Acylcarnitine profile
	Plasma methylmalonic acid (MMA)
Initial Diagnostics at Referral Center	Plasma amino acids
	Total homocysteine
	$B_{12}$ levels in patient and mother
	Electrolytes (especially if sick)
Recommended additional testing to consider	Blood glucose Ammonia
at time of initial consultation	
·	Carnitine, total and free
	Urine ketones
	Elevated methylmalonic acid with or without elevated 3-OH-
	propionic acid and methylcitric acid (UOA)
	Elevated C3/C4DC
	Normal amino acids (may have elevated glycine)
Abnormal Metabolites Expected	Normal total homocysteine and B <sub>12</sub> levels
Tienerman Hetaeetties Expected	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
	Ammonia can be elevated in sick patients
	Normal/low carnitine levels
	Elevated urine ketones, especially in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Elevated methylmalonic acid in blood and urine
	Mutation analysis:
	0 mutation - disease ruled out (unless consanguineous)
	1 mutation - proceed to enzyme assay
	2 mutations in trans – diagnosis confirmed
	Complementation studies in fibroblasts
Differential Diagnosis	Cobalamin C Cofactor Deficiency (Cbl C); Cobalamin D <sub>2</sub>
	Cofactor Deficiency (Cbl D <sub>2</sub> ); Methylmalonic-CoA Mutase
	Deficiency (MUT); Propionic Acidemia (PA); Succinate-CoA
	Ligase, beta subunit (SUCLA <sub>2</sub> ); Succinate-CoA Ligase, alpha
	subunit (SUCLG <sub>1</sub> )
	Subulif (SUCLO])

Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1848552%5BDISCUI %5D&condition=C1848552&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1328/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C3.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

## Methylmalonic Aciduria - Cobalamin C Cofactor Deficiency (Cbl C); Cobalamin D<sub>2</sub> Cofactor Deficiency (Cbl D<sub>2</sub>), Cobalamin F Cofactor Deficiency (Cbl F); Cobalamin J Cofactor Deficiency (Cbl J)

(Organic Acidemia)

	Tame neuclina)
Disease (common abbreviation)	Methylmalonic Aciduria - Cobalamin C Cofactor Deficiency
	(Cbl C); Cobalamin D <sub>2</sub> Cofactor Deficiency (Cbl D <sub>2</sub> );
	Cobalamin F Cofactor Deficiency (Cbl F); Cobalamin J
	Cofactor Deficiency (Cbl J)
	277400, 277410, 277380
	74653006; 31220004 / E71.120
	MTHF methyltransferase (Cobalamin C cofactor)
MIM#	609831
SNOMED Code / ICD-10-CM Code	MMADHC protein (Cobalamin D <sub>2</sub> cofactor)
Enzyme or other abnormality	611935 / 5.4.99.2; None
MIM#	LMBRD1 (Cobalamin F cofactor) 612625 /
/Enzyme Commission #	Cobalamin J cofactor not found in OMIM
/ Lnzyme Commission #	Elevated C3
Abraganal Nambara Caragaire a Matabalita(a)	53160-8
Abnormal Newborn Screening Metabolite(s)	
LOINC Number(s)	Elevated C4DC
	45222-7 (?low methionine in some states)
	Urine organic acids (UOA)
	Plasma acylcarnitine profile
Initial Diagnostics at Referral Center	Plasma methylmalonic acid (MMA)
Timum Diagnosties at Rejerral Center	Plasma amino acids (PAA)
	Total homocysteine
	B12 levels in patient and mother
	Electrolytes (especially if sick)
Basemmanded additional testing to consider	Blood glucose
Recommended additional testing to consider	Ammonia
at time of initial consultation	Carnitine, total and free
	Urine ketones
	Elevated total homocysteine
	Elevated MMA (UOA)
	Normal amino acids (may have elevated free homocystine and
	low methionine) (PAA)
	Normal/elevated B <sub>12</sub> levels
Abnormal Metabolites Expected	Electrolyte abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
	Ammonia can be elevated in sick patients
	Normal/low carnitine levels
	Elevated urine ketones, especially in sick patients
If initial testing is negative has the disorder	Lie valed urine retories, especially in sier patients
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Elevated total plasma homocysteine and elevated
	methylmalonic acid in blood and urine
	Mutation analysis:
	0 mutation - disease ruled out (unless consanguineous)
	1 mutation - proceed to enzyme assay
	2 mutations in trans confirms diagnosis.
	- materions in train continue diagnosis.

	Complementation studies in fibroblasts
Differential Diagnosis	Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D <sub>1</sub> Cofactor Deficiency (Cbl D <sub>1</sub> ); Methylmalonic-CoA Mutase Deficiency (MUT); Propionic Acidemia (PA)
Specific Testing Laboratories as listed in the Genetic Testing Registry	CblC: www.ncbi.nlm.nih.gov/gtr/tests/?term=C1848561%5BDISCUI %5D&condition=C1848561&compare_labs=1 Cbld <sub>2</sub> : www.ncbi.nlm.nih.gov/gtr/tests/?term=C1848552%5BDISCUI %5D&condition=C1848552&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1328/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C3.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

### Multiple Carboxylase Deficiency (MCD) (Organic Acidemia)

Disease (common abbreviation)	Multiple Carboxylase Deficiency (MCD)
MIM#	253270
SNOMED Code / ICD-10-CM Code	15307001 / D81.81
Enzyme or other abnormality	Holocarboxylase synthetase (HCS)
MIM # / Enzyme Commission #	609018 / 6.3.4.11
,	Elevated C3
Abnormal Newborn Screening Metabolite(s)	53160-8
LOINC Number(s)	Elevated C5OH
	45207-8
	Urine organic acid (UOA)
	Plasma Acylcarnitine profile
Initial Diagnostics at Referral Center	Biotinidase assay if not done by state newborn screening
	program
	Lactate
Recommended additional testing to consider	Electrolytes
at time of initial consultation	Glucose
at time of tititual constitution	Ammonia
	Elevated 3-OH-isovaleric acid, lactate, tiglylglycine, 3-
	methylcrotonylglycine, methylcitrate, 3-OH propionate
	(UOA)
Abnormal Metabolites Expected	Elevated C5OH and C3 (plasma acylcarnitines)
Tienerman Menaethies Expected	Elevated lactate in sick patients
	Electrolyte abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
	Ammonia can be elevated in sick patients
If initial testing is negative has the disorder	Yes
been ruled out?	
	Mutation analysis:
	0 mutation - disease unlikely (unless consanguineous)
Diagnostic Confirmation	1 mutation - proceed to enzyme assay
	2 known or likely pathological mutations in trans confirms
	diagnosis Engume analysis in fibrablests and lymphosytes
	Enzyme analysis in fibroblasts and lymphocytes  Pictinidase Deficiency 2 Methylerotoxylekvinynia (2MCC)
Differential Diagnosis	Biotinidase Deficiency; 3-Methylcrotonylglycinuria (3MCC);
	Propionic Acidemia (PA); Pyruvate Carboxylase Deficiency
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268581%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268581&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C5-OH.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-
Algorithm	<u>OH.pdf</u>
Recommended Uniform Screening Panel (RUSP)	Core Panel

### Methylmalonyl-CoA Mutase Deficiency (MUT) (Organic Acidemia)

Disease (common abbreviation) MIM #	Methylmalonyl-CoA Mutase Deficiency (MUT) 251000
SNOMED Code / ICD-10-CM Code	124680001 / E71.120
Enzyme or other abnormality	Methylmalonyl-CoA mutase
MIM # / Enzyme Commission #	251000 / 5.4.99.2
	Elevated C3
Abnormal Newborn Screening Metabolite(s)	53160-8
LOINC Number(s)	Elevated C4DC
	45222-7
	Urine organic acids (UOA)
	Plasma Acylcarnitine profile
Initial Diggressing at Performal Contan	Plasma methylmalonic acid
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
	Total homocysteine
	B <sub>12</sub> levels in patient and mother
	Electrolytes (especially if sick)
	Blood glucose
Recommended additional testing to consider	Ammonia
at time of initial consultation	Carnitine, total and free
	Urine ketones
	Elevated methylmalonic acid (UOA and in plasma)
	Elevated 3-OH-propionic acid, methylcitric acid, (UOA)
	Elevated 3-Ori-proprofile acid, flictifyletific acid, (OOA)
Abu ayun al Matabalitas Eymaatad	Normal homocysteine and B <sub>12</sub> levels
Abnormal Metabolites Expected	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
	Ammonia can be elevated in sick patients
	Normal/low carnitine levels
	Elevated urine ketones especially in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
	Mutation analysis:
	0 mutation disease unlikely (unless consanguineous)
D:	1 mutation - proceed to enzyme assay
Diagnostic Confirmation	2 known or likely pathological mutations in trans confirms
	diagnosis
	Complementation studies in fibroblasts
	Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D <sub>1</sub> Variant
Differential Diagnosis	(Cbl D <sub>1</sub> ); Cobalamin C Cofactor Deficiency (Cbl C) (normal
	or increased homocysteine); Cobalamin D <sub>2</sub> Cofactor
	Deficiency (Cbl D <sub>2</sub> ) (increased homocysteine); Propionic
	Acidemia (PA)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1855114%5BDISCUI
Genetic Testing Registry	%5D&condition=C1855114&compare_labs=1
, ,	*
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C3.pdf

Sheet	
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

### Propionic Acidemia (PA) (Organic Acidemia)

· ·	rgame Acidema)
Disease (common abbreviation)	Propionic Acidemia (PA)
MIM#	606054
SNOMED Code / ICD-10-CM Code	69080001 / E71.121
Enzyme or other abnormality	Propionyl-CoA carboxylase
MIM # / Enzyme Commission #	232000, 232050 / 6.4.1.3
Abnormal Newborn Screening Metabolite(s)	Elevated C3
LOINC Number(s)	53160-8
	Urine organic acids (UOA)
	Plasma Acylcarnitine profile
Initial Diagnostics at Referral Center	Plasma methylmalonic acid
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
	Total homocysteine
	B12 levels in patient and mother
	Electrolytes (especially if sick)
D	Glucose
Recommended additional testing to consider	Ammonia
at time of initial consultation	Carnitine, total and free
	Urine ketones
	Elevated 3-OH-propionate, propionylglycine, tiglylglycine,
	propionate(volatile, so not always detected) and methylcitrate
	(UOA)
	Elevated glycine (PAA)
	Normal methylmalonic acid and homocysteine
Abnormal Metabolites Expected	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
	Ammonia can be elevated in sick patients
	Normal/low carnitine levels
	Elevated urine ketones especially in sick patients
If initial testing is negative has the disorder	· · ·
been ruled out?	Yes
	Elevated propionate and methylcitrate generally accepted for
Diagnostic Confirmation	diagnosis
	Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D <sub>1</sub> Variant
Differential Diagnosis	(Cbl D <sub>1</sub> ); Cobalamin C Cofactor Deficiency (Cbl C);
Dijjerenilai Diagnosis	
Consider Testine I showed with a line that I in the	Methylmalonic-CoA Mutase Deficiency (MUT)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268579%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268579&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK92946/
American College of Medical Genetics ACT	
Sheet	www.acmg.net/StaticContent/ACT/C3.pdf
American College of Medical Genetics	. (G), G
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3.pdf
(RUSP)	Core Panel
Recommended Uniform Screening Panel	Core Panel
(NOSI)	

### Beta-Oxothiolase Deficiency; Beta-Ketothiolase Deficiency (BKT) (Organic Acidemia)

(Organic Acidemia)	
Disease (common abbreviation)	Beta-Oxothiolase Deficiency; Beta-Ketothiolase Deficiency
	(BKT)
MIM #	203750
SNOMED Code / ICD-10-CM Code	237953006 / E71.19
Enzyme or other abnormality	Beta-ketothiolase (mitochondrial acetoacetyl-CoA lyase)
MIM # / Enzyme Commission #	607809 / 2.3.1.16
Abnormal Newborn Screening Metabolite(s)	Elevated C5:1
LOINC Number(s)	53170-7
LOTIVE Trumber(s)	Elevated C5OH
Initial Diagnostics at Referral Center	Urine organic acids
Initial Diagnostics at Rejerral Center	Plasma Acylcarnitine profile
Recommended additional testing to consider	Electrolytes
at time of initial consultation	Blood glucose
	Elevated urinary tiglylglycine, 2-methyl-3OH-butyrate and 2-
	methylacetoacetate (UOA)
Alexandra I. M. a. I. d. a. E. a. a. d. I.	Elevated tiglylcarnitine and 2-methyl-3-OH-butyrylcarnitine
Abnormal Metabolites Expected	(Acylcarnitine)
	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder	No
been ruled out?	110
	Enzyme assay
	Mutation analysis:
Diagnostic Confirmation	0 mutation - disease unlikely (unless consanguineous)
Diagnostic Confirmation	1 mutation - proceed to enzyme assay
	2 known or likely pathological mutations in trans confirms
	diagnosis
Differential Diagnosis	2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase Deficiency
Differential Diagnosis	(MHBD)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1536500%5BDISCUI
Genetic Testing Registry	%5D&condition=C1536500&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C5-OH.pdf
Sheet	www.acmg.net/StaticContent/AC1/C3-O11.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-
Algorithm	OH.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

### Glutaric Acidemia Type 1 (GA-I) (Organic Acidemia)

	rgame Acidemia)
Disease (common abbreviation)	Glutaric Acidemia Type I (GA-I)
MIM #	231670
SNOMED Code / ICD-10-CM Code	76175005 / E72.3
Enzyme or other abnormality	Glutaryl-CoA dehydrogenase
MIM # / Enzyme Commission #	608801 / 1.3.99.7
Abnormal Newborn Screening Metabolite(s)	Elevated C5DC
LOINC Number(s)	45207-8
	Urine organic acids (UOA)
Initial Diagnostics at Referral Center	Plasma Acylcarnitine profile
	Urine glutarylcarnitine
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Urine glutaric and 3-OH-glutaric acid by stable isotope dilution
ai une of initial consultation	Carnitine, total and free
	Elevated 3-OH-glutaric acid
	+/- glutaric acid (UOA)
Abnormal Metabolites Expected	Elevated glutarylcarnitine (plasma and urine)
Aonormai Meiavoines Expeciea	Blood glucose depends on fed status of patient
	Elevated glutaric and 3-OH glutaric levels
	Normal/low carnitine levels
If initial testing is negative has the disorder been ruled out?	Yes (in most cases)
	Persistently elevated 3-OH-glutaric acid
	Mutation analysis:
Diagnostic Confirmation	0 mutation disease unlikely (unless consanguineous)
Diagnostic Confirmation	1 mutation - proceed to enzyme assay
	2 known or likely pathological mutations in trans confirms
	diagnosis
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268595%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268595&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C5-DC.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/C5-
Algorithm	<u>DC_(4_29_06).pdf</u>
Recommended Uniform Screening Panel (RUSP)	Core Panel

### 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG) (Organic Acidemia)

(Organic Actuenta)	
Disease (common abbreviation)	3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG)
MIM #	246450
SNOMED Code / ICD-10-CM Code	124611007 / E71.19
Enzyme or other abnormality	3-Hydroxy-3-Methylglutaryl-CoA Lyase
MIM # / Enzyme Commission #	246450 / 4.1.3.4
	Elevated C5OH
Abnormal Newborn Screening Metabolite(s)	50106-4
LOINC Number(s)	Elevated C6DC
	53187-1
Listial Diagnostics at Defend Contan	Urine organic acids (UOA)
Initial Diagnostics at Referral Center	Plasma acylcarnitine profile
Recommended additional testing to consider	Electrolytes
at time of initial consultation	Blood glucose
	Elevated 3-hydroxyisovaleric acid, 3-methylglutaconic acid, 3-
	methylglutaric acid, 3-hydroxy-3-methylglutarate (UOA)
Abnormal Metabolites Expected	Elevated C5OH, C6DC
Honormai Metabotties Expected	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder	<u> </u>
been ruled out?	Yes
Diagnostic Confirmation	Abnormal metabolite pattern confirms diagnosis
	3-Methylcrotonylglycinuria aka 3-Methylcrotonyl-CoA
Differential Diagnosis	Carboxylase Deficiency (3MCC); 3-Methylglutaconic
	Aciduria (3MGA)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268601%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268601&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	VIG. 1. G. A. ALAGRIGA OTT. 10
Sheet	www.acmg.net/StaticContent/ACT/C5-OH.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-
Algorithm	OH.pdf
Recommended Uniform Screening Panel	Core Panel
(RUSP)	

### 3-Methylcrotonylglycinuria; 3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC) (Organic Acidemia)

Disease (common abbreviation)	3-Methylcrotonylglycinuria; Methylcrotonyl-CoA Carboxylase
	Deficiency (3MCC)
MIM #	210200, 210210
SNOMED Code / ICD-10-CM Code	13144005 / E71.19
Enzyme or other abnormality	3-Methylcrotonyl-CoA carboxylase
MIM # / Enzyme Commission #	609010, 609014 / 6.4.1.4
Abnormal Newborn Screening Metabolite(s)	Elevated C5OH
LOINC Number(s)	50106-4
	Urine organic acid analysis (UOA)
Initial Diagnostics at Referral Center	Plasma acylcarnitine profile
	Maternal testing of same analytes at time of initial evaluation
Recommended additional testing to consider at time of initial consultation	None
	Elevated 3-hydroxyisovaleric acid and 3-methylcrotonylglycine
Abnormal Metabolites Expected	(UOA)
Abnormai Meiaboilles Expected	Elevated C5OH
	*Maternal testing may indicate 3MCC
If initial testing is negative has the disorder been ruled out?	Yes (Consider maternal 3MCC)
	Elevated C5OH and 3-methylcrotonylglycine
Diagnostic Confirmation	Enzyme analysis in lymphocytes or fibroblasts
	Mutation analysis
Differential Diagnosis	3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG); 3-Methylglutaconic Aciduria (3MGA)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268600%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268600&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C5-OH.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-
Algorithm	<u>OH.pdf</u>
Recommended Uniform Screening Panel	Core Panel
(RUSP)	

#### 3-Methylglutaconic Aciduria Type I (3MGA I) (Organic Acidemia)

(Organic Acidenna)	
Disease (common abbreviation)	3-Methylglutaconic Aciduria Type I (3MGA I)
MIM #	250950
SNOMED Code / ICD-10-CM Code	237950009 / E71.111
Enzyme or other abnormality	3-Methylglutaconyl-CoA hydratase
MIM # / Enzyme Commission #	600529 / 4.2.18
Abnormal Newborn Screening Metabolite(s)	Elevated C5OH
LOINC Number(s)	50106-4
Lidial Diagram of Bafamal Contac	Urine organic acids
Initial Diagnostics at Referral Center	Plasma Acylcarnitine profile
Recommended additional testing to consider	Electrolytes
at time of initial consultation	Blood glucose
Abnormal Metabolites Expected	Elevated 3-methylglutaconic acid, 3-methylglutaric acid and 3-hydroxyisovaleric acid (UOA) Elevated C5OH
•	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder been ruled out?	Yes (consider maternal 3MGA)
Diagnostic Confirmation	Mutation analysis is available
Differential Diagnosis	3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG); 3-Methylcrotonylglycinuria aka 3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC); 3-Methylglutaconic Aciduria, Type I (3MGA II); 3-Methylglutaconic Aciduria, Type I (3MGA IV)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342727%5BDISCUI
Genetic Testing Registry	%5D&condition=C0342727&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C5-OH.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-OH.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

#### Isovaleric Acidemia (IVA) (Organic Acidemia)

(0	rganic Acidenna)
Disease (common abbreviation)	Isovaleric Acidemia (IVA)
MIM#	243500
SNOMED Code / ICD-10-CM Code	87827003 / E71.110
Enzyme or other abnormality	Isovaleryl-CoA dehydrogenase
MIM # / Enzyme Commission #	607036 / 1.3.99.10
Abnormal Newborn Screening Metabolite(s)	Elevated C5
LOINC Number(s)	45216-9
	Urine organic acids (UOA)
Initial Diagnostics at Referral Center	Plasma Acylcarnitine profile
	Urine acylglycines
	Electrolytes
Recommended additional testing to consider	Urine ketones
at time of initial consultation	Blood glucose
	Ammonia
	Elevated isovalerylglycine, isovaleric acid and 3-OH-isovaleric
	acid (UOA)
	Elevated isovalerylcarnitine (C5)
Abnormal Metabolites Expected	Elevated isovalerylglycine
Abnormai Meiaboines Expeciea	Electrolytes abnormalities are common in sick patients
	Elevated urine ketones especially in sick patients
	Blood glucose depends on fed status of patient
	Ammonia can be elevated in sick patients
If initial testing is negative has the disorder	Yes
been ruled out?	168
Diagnostic Confirmation	Elevated isovalerylglycine, <u>absent</u> 2-methylbutyrlglycine
Differential Diagnosis	2-Methylbutyryl Glycinuria (2MBG)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268575%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268575&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C5.pdf
Sheet	www.ucing.nevounceontent/101/03.pui
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5.pdf
Algorithm	www.acmg.nevoauteContent/1C1/11gortums/v1sto-C5.put
Recommended Uniform Screening Panel	Core Panel
(RUSP)	0010 1 41101

### Malonic Aciduria (MA) (Organic Acidemia)

Disease (common abbreviation)	Malonic Aciduria (MA)
MIM#	248360
SNOMED Code / ICD-10-CM Code	124594007 / E71.39
Enzyme or other abnormality	Malonyl-CoA Decarboxylase (MLYCD)
MIM # / Enzyme Commission #	606761 / 4.1.1.9
Abnormal Newborn Screening Metabolite(s)	Elevated C3DC
LOINC Number(s)	54462-7
	Urine organic acids (UOA)
Initial Diagnostics at Referral Center	Plasma Acylcarnitine profile
Recommended additional testing to consider at time of initial consultation	Urine ketones
	Elevated malonic acid, methylmalonic acid, and dicarboxylic
	acids (UOA)
Abnormal Metabolites Expected	Abnormal succinic acid in 50% of patients (UOA)
	Elevated C3DC
	Elevated urine ketones especially in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
	Persistent elevation of malonic acid level greater than
Diagnostic Confirmation	methylmalonic acid level
	Mutation analysis available
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342793%5BDISCUI
Genetic Testing Registry	%5D&condition=C0342793&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C3-DC.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3-
Algorithm	<u>DC.pdf</u>
Recommended Uniform Screening Panel (RUSP)	Secondary Target

### 2-Methylbutyryl Glycinuria (2MBG) (Organic Acidemia)

,	rgaine Acidenna)
Disease (common abbreviation)	2-Methylbutyryl Glycinuria (2MBG)
MIM#	600301
SNOMED Code / ICD-10-CM Code	None / E71.19
Enzyme or other abnormality	2-Methylbutyryl-CoA dehydrogenase
MIM # / Enzyme Commission #	600301 / 1.3.99.12
Abnormal Newborn Screening Metabolite(s)	Elevated C5
LOINC Number(s)	45216-9
	Urine organic acids
Initial Diagnostics at Referral Center	Plasma acylcarnitine profile
	Urine acylglycines
	Electrolytes
Recommended additional testing to consider	Urine ketones
at time of initial consultation	Blood glucose
	Ammonia
	Elevated 2-methylbutyrylglycine (UOA and UAG)
	Elevated C5
Al.,	Electrolytes abnormalities are common in sick patients
Abnormal Metabolites Expected	Elevated urine ketones especially in sick patients
	Blood glucose depends on fed status of patient
	Ammonia can be elevated in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Elevated 2-methylbutrylglycine
Diagnostic Confirmation	Mutation analysis
Differential Diagnosis	Isovaleric Acidemia (IVA)
Specific Testing Laboratories as listed in the Genetic Testing Registry	None
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C5.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

### 2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase Deficiency (2M3HBA) (Organic Acidemia)

(0	rganic Acidenna)
Disease (common abbreviation)	2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase Deficiency
MIM //	(2M3HBA)
MIM#	300438
SNOMED Code / ICD-10-CM Code	None / E71.19
Enzyme or other abnormality	2-Methyl-3-hydroxybutyryl-CoA dehydrogenase
MIM # / Enzyme Commission #	300256 / 1.1.178
Abnormal Newborn Screening Metabolite(s)	Elevated C5:1
LOINC Number(s)	53170-7
Lonve ivaniber(s)	Elevated C5OH
Initial Diagnostics at Patarval Contar	Urine organic acids
Initial Diagnostics at Referral Center	Plasma Acylcarnitine profile
Recommended additional testing to consider	Electrolytes
at time of initial consultation	Blood glucose
	Elevated 2-methyl-3-hydroxybutyrate and tiglylglycine without
	elevation of 2-methylacetoacetate (UOA)
Abnormal Metabolites Expected	Elevated C5:1- and C5OH
	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder been ruled out?	No
	Mutation analysis:
	0 mutation - disease unlikely (unless consanguineous)
	1 mutation - proceed to enzyme assay
Diagnostic Confirmation	2 known or likely pathological mutations in trans confirms
	diagnosis
	Enzyme analysis
	Beta-Oxothiolase Deficiency aka Beta-Ketothiolase Deficiency
Differential Diagnosis	(BKT)
Consider Testing Laboratories and Listed 1: 11	
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1845517%5BDISCUI
Genetic Testing Registry	%5D&condition=C1845517&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C5-OH.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-
Algorithm	OH.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target
(RODI)	

### Biotinidase Deficiency (BIOT) (Other Genetic Condition)

	Genetic Condition)
Disease (common abbreviation)	Biotinidase Deficiency (BIOT)
MIM #	253260
SNOMED Code / ICD-10-CM Code	8808004 / D81.810
Enzyme or other abnormality	Biotinidase
MIM # / Enzyme Commission #	609019 / 3.5.1.12
Abnormal Newborn Screening Metabolite(s)	Decreased biotinidase activity
LOINC Number(s)	38478-4
Initial Diagnostics at Referral Center	Quantitative serum biotinidase activity
Recommended additional testing to consider at time of initial consultation	Urine organic acids
Al	Decreased biotinidase activity
Abnormal Metabolites Expected	Urine organic acids are usually normal in the neonatal period
If initial testing is negative has the disorder	Yes
been ruled out?	1 es
Diagnostic Confirmation	Decreased or absent biotinidase activity in serum
Differential Diagnosis	Multiple Carboxylase Deficiency (MCD/ Holocarboxylase
Differential Diagnosis	Synthetase Deficiency (HCS)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0220754%5BDISCUI
Genetic Testing Registry	%5D&condition=C0220754&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1322/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Biotinidase.pdf
Sheet	www.acmg.net/StaticContent/AC1/Biotinidase.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Biotinidase.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

## Cystic Fibrosis (CF) (Other Genetic Condition)

(Other Genetic Condition)	
Cystic Fibrosis (CF)	
219700	
190905008 / E84	
Cystic fibrosis transmembrane receptor (CFTR)	
602421 / None	
Elevated immunoreactive trypsinogen (IRT)	
48633-2	
Presence or absence of CFTR mutations	
54083-1	
Sweat test and confirmation of mutations detected on newborn	
screening (if done)	
Mutation analysis of the CFTR gene	
Elevated sweat chloride >60 millieq/L	
Pathologic CFTR mutations	
Yes for classical cases	
Borderline sweat test range of 30-60 millieq/L may represent an	
intermediate phenotype and require further testing	
Repeat sweat test and/or genetic analysis, especially if infant	
shows clinical symptoms	
None	
http://www.ncbi.nlm.nih.gov/gtr/tests/?term=1080[geneid]&co	
ndition=C0010674&compare_labs=1	
www.ncbi.nlm.nih.gov/books/NBK1250/	
The state of the s	
www.acmg.net/StaticContent/ACT/CF.pdf	
www.comc.not/StaticContent/ACT/Algorithme/Wisis_IDT = 4f	
www.acmg.net/StaticContent/ACT/Algorithms/Visio-IRT.pdf	
Core Panel	

### Classical Galactosemia (GALT) (Other Genetic Condition)

	er Geneuc Condition)
Disease (common abbreviation)	Classical Galactosemia (GALT)
MIM #	230400
SNOMED Code / ICD-10-CM Code	398664009 / E74.21
Enzyme or other abnormality	Galactose-1-Phosphate Uridyltransferase
MIM # / Enzyme Commission #	606999 / 2.7.7.12
	Decreased GALT activity
Abramal Nauham Caramina Matabalita(a)	33288-2 (presence) 42906-8 (activity/volume)
Abnormal Newborn Screening Metabolite(s)	Common mutation analysis (some states)
LOINC Number(s)	Elevated total galactose in some states
	54084-9
	RBC Galactose-1-phosphate (Gal-1-P)
Initial Diagnostics at Referral Center	RBC GALT activity
D 11 1111 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Liver function tests
Recommended additional testing to consider	Urine reducing substances
at time of initial consultation	Urine galactitol
	Elevated Gal-1-P
	Decreased GALT activity
Abnormal Metabolites Expected	Liver function tests may be abnormal in sick patients
	Elevated urine reducing substances
	Elevated urine galactitol
If initial testing is negative has the disorder	If GALT activity normal proceed to galactokinase and
been ruled out?	epimerase testing in states that report elevated galactose
been ruieu oui:	
Diagnostic Confirmation	Decreased GALT activity
J J	Mutation analysis of the GALT gene
Differential Diagnosis	Galactokinase Deficiency (GALK); Galactose Epimerase
	Deficiency (GALE)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268151%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268151&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1518/
	GALT:
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/GalactosePlusGALT.pdf
Sheet	Elevated Galactose + deficient GALT:
	www.acmg.net/StaticContent/ACT/Galactose.pdf
	GALT:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
American College of Medical Genetics Algorithm	GALT.pdf
	Elevated Galactose + deficient GALT:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Hypergalactosemia.pdf
Recommended Uniform Screening Panel	
(RUSP)	Core Panel
(NODI)	

### Galactokinase Deficiency (GALK) (Other Genetic Condition)

,	Genetic Condition)
Disease (common abbreviation)	Galactokinase Deficiency (GALK)
MIM #	230200
SNOMED Code / ICD-10-CM Code	124302001 / E74.29
Enzyme or other abnormality	Galactokinase
MIM # / Enzyme Commission #	604313 / 2.7.1.6
Abnormal Newborn Screening Metabolite(s)	Elevated galactose in some states
LOINC Number(s)	54084-9
Eonte itumoer(s)	Normal GALT
	RBC Galactose-1-phosphate (Gal-1-P)
Initial Diagnostics at Referral Center	RBC Galactose-1-phosphate uridyltransferase (GALT) activity
	(testing for galactokinase done after testing for GALT)
Recommended additional testing to consider	Liver function tests
at time of initial consultation	Urine reducing substances
at time of titital constitution	Urine galactitol
	Normal Gal-1-P
	Normal GALT
Abnormal Metabolites Expected	Normal liver function tests
	Elevated urine reducing substances
	Elevated urine galactitol
If initial testing is negative has the disorder	If GALT activity normal proceed to galactokinase and
been ruled out?	epimerase testing in states that report elevated galactose
	RBC galactokinase activity
Diagnostic Confirmation	Mutation analysis in suspected cases
	Galactosemia (GALT); Galactose Epimerase Deficiency
Differential Diagnosis	(GALE)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268155%5BDISCUI
Genetic Testing Registry	%5D&condition=C0268155&compare labs=1
, ,	_
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1518/
American College of Medical Genetics ACT	Elevated Galactose +/- deficient GALT:
Sheet	www.acmg.net/StaticContent/ACT/Galactose.pdf
	Elevated Galactose +/- deficient GALT:
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Hypergalactosemia.pdf
Recommended Uniform Screening Panel	
(RUSP)	Secondary Target
,	I .

### Galactose Epimerase Deficiency (GALE) (Other Genetic Condition)

(Omer General Controlly)	
Disease (common abbreviation)	Galactose Epimerase Deficiency (GALE)
MIM #	230350
SNOMED Code / ICD-10-CM Code	8849004 / E74.21
Enzyme or other abnormality	UDP-galactose-4-epimerase
MIM # / Enzyme Commission #	606953 / 5.1.3.2
Abnormal Newborn Screening Metabolite(s)	Elevated galactose in some states
LOINC Number(s)	54084-9
	Galactose-1-phosphate (Gal-1-P)
Initial Diagnostics at Referral Center	Galactose-1-phosphate uridyltransferase (GALT) activity
	(testing for epimerase deficiency done after testing for GALT)
Recommended additional testing to consider	Liver function tests
at time of initial consultation	Urine reducing substances
ai une of initial consultation	Urine galactitol
	Elevated Gal-1-P
	Normal GALT
Abnormal Metabolites Expected	Normal liver function tests
	Elevated urine reducing substances
	Elevated urine galactitol
If initial testing is negative has the disorder	If GALT activity normal proceed to galactokinase and
been ruled out?	epimerase testing in states that report elevated galactose
Diagnostic Confirmation	RBC epimerase activity
Differential Diagnosis	Galactosemia; Galactokinase Deficiency (GALK)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0751161%5BDISCUI
Genetic Testing Registry	%5D&condition=C0751161&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK51671/
American College of Medical Genetics ACT	Elevated Galactose +/- deficient GALT:
Sheet	www.acmg.net/StaticContent/ACT/Galactose.pdf
American College of Medical Genetics Algorithm	Elevated Galactose +/- deficient GALT:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	<u>Hypergalactosemia.pdf</u>
Recommended Uniform Screening Panel	Secondary Target
(RUSP)	Secondary Target

### T-cell-related Lymphocyte Deficiencies: Severe Combined Immunodeficiency (SCID); (Other Genetic Condition)

(Other Genetic Condition)	
Disease (common abbreviation)	T-cell-related Lymphocyte Deficiencies: Severe Combined
	Immunodeficiency (SCID)
MIM #	Many
SNOMED Code / ICD-10-CM Code	31323000/D81.1
Enzyme or other abnormality	
MIM # / Enzyme Commission #	
Abnormal Newborn Screening Metabolite(s)	
	T-Cell Receptor Excision Circles (TREC)
LOINC Number(s)	
Initial Diagnostics at Referral Center	Flow cytometry measuring the absolute number of T-cells, B-cells and NK cells
Becommended additional testing to consider	Repeat Newborn Screen (especially in premature infants),
Recommended additional testing to consider	Lymphocyte proliferation to mitogens, T-cell subsets (naïve,
at time of initial consultation	memory and activated)
Abnormal Metabolites Expected	Low T cell number, variable B and NK cells numbers
Abnormai Meiaboines Expeciea	depending on SCID etiology
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Varies by SCID subtype, needs referral to Specialty Center
	Many SCID subtypes and other immunodeficiencies are
	associated with T-cells lymphopenia. Chromosome 22q11
Differential Diagnosis	deletion syndrome (DiGeorge syndrome) is a common
Differential Diagnosis	differential diagnosis. Premature infants without a hereditary
	immunodeficiency are also more likely to have low TREC
	values.
Specific Testing Laboratories as listed in the	http://www.nchi.nlm.nih.gov/gtr/tosts/2torm_C0095110FDISCII
Specific Testing Laboratories as listed in the Genetic Testing Registry	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=C0085110[DISCU] []&condition=C0085110&compare_labs=1
Geneue Testing Registry	1
	X-SCID http://www.ncbi.nlm.nih.gov/books/NBK1410/,
GeneReviews	ADA Deficiency
	http://www.ncbi.nlm.nih.gov/books/NBK1483/,
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/SCID.pdf
Sheet	www.acmg.net/StaticContent/ACT/SCID.pui
American College of Medical Genetics	In development
Algorithm	in de velopinent
Recommended Uniform Screening Panel	Core
(RUSP)	

### Fabry Disease (Lysosomal Storage Disorder)

(2)5050	(Lysosomai Storage Disorder)	
Disease (common abbreviation)	Fabry Disease	
MIM #	301500	
SNOMED Code / ICD-10-CM Code	16652001/E75.21	
Enzyme or other abnormality	Alpha-galactosidase A (α-Gal A)	
MIM # / Enzyme Commission #	300644 / 3.2.1.22	
Abnormal Newborn Screening Metabolite(s)	Decreased α-Gal A activity	
LOINC Number(s)	62304-1	
Initial Diagnostics at Referral Center	Repeat α-Gal A activity	
Recommended additional testing to consider at time of initial consultation	None	
Abnormal Metabolites Expected	Decreased α-Gal A activity	
If initial testing is negative has the disorder been ruled out?	Yes	
Di di Ci di	Deficient α-Gal A activity	
Diagnostic Confirmation	GLA mutation analysis on non-urgent basis	
Differential Diagnosis	None	
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0002986%5BDISCUI	
Genetic Testing Registry	%5D&condition=C0002986&compare_labs=1	
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1292/	
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Fabry.pdf	
Sheet		
American College of Medical Genetics	In development	
Algorithm	r	
Recommended Uniform Screening Panel (RUSP)	Not on Panel	

### Niemann-Pick Disease Types A & B; Acid Sphingomyelinase (ASM) Deficiency (Lysosomal Storage Disorder)

. •	mu Storage Disoraci)
Disease (common abbreviation)	Niemann-Pick Disease Types A & B; Acid Sphingomyelinase
	(ASM) Deficiency
MIM #	257200
SNOMED Code / ICD-10-CM Code	52165006 (Type A), 39390005 (Type B) /
	E75.240 (Type A), E75.241 (Type B)
Enzyme or other abnormality	Acid sphingomyelinase (ASM)
MIM # / Enzyme Commission #	607608 / 3.1.4.12
Abnormal Newborn Screening Metabolite(s)	Deficient ASM activity
LOINC Number(s)	62315-7
Luitial Diagnostics at Reformal Conton	Repeat ASM activity
Initial Diagnostics at Referral Center	Mutation analysis of SMPD1
Recommended additional testing to consider	None
at time of initial consultation	None
Abnormal Metabolites Expected	Deficient ASM activity
If initial testing is negative has the disorder	Yes
been ruled out?	168
Diagnostic Confirmation	ASM activity <10%
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0028064%5BDISCUI
Genetic Testing Registry	%5D&condition=C0028064&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1370/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/NiemannPick.pdf
Sheet	
American College of Medical Genetics	In development
Algorithm	in do , otopinone
Recommended Uniform Screening Panel	Not on Panel
(RUSP)	110t Oil 1 diloi

# Gaucher Disease; Glucocerebrosidase Deficiency; Glucosylceramidase Deficiency, not including Saposin C Deficiency (Lysosomal Storage Disorder)

	and storage Districtly
	Gaucher Disease (GD); Glucocerebrosidase Deficiency;
Disease (common abbreviation)	Glucosylceramidase Deficiency, not including Saposin C
MIM #	Deficiency
SNOMED Code / ICD-10-CM Code	231000
Enzyme or other abnormality	12246008/E75.22
MIM # / Enzyme Commission #	Glucocerebrosidase
	606463/3.2.1.45
Abnormal Newborn Screening Metabolite(s)	Deficient glucocerebrosidase activity
LOINC Number(s)	62311-6
1 /	If no family history, repeat enzyme activity and perform GBA
Listial Diggraphics at Reformal Contan	mutation analysis.
Initial Diagnostics at Referral Center	If positive family history with known mutation, perform GBA
	mutation analysis.
Recommended additional testing to consider	None
at time of initial consultation	None
Abnormal Metabolites Expected	Deficient glucocerebrosidase activity
If initial testing is negative has the disorder	?Yes
been ruled out?	: 105
Diagnostic Confirmation	Deficient glucocerebrosidase activity
Differential Diagnosis	None
Specific Testing Laboratories as listed in	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=Glucosylceramida
GeneTests	se Deficiency&condition=C0017205&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1269/
American College of Medical Genetics ACT	www.someonst/StatioContent/ACT/Conshormalf
Sheet	www.acmg.net/StaticContent/ACT/Gaucher.pdf
American College of Medical Genetics	In davidonment
Algorithm	In development
Recommended Uniform Screening Panel	Not on Panel
(RUSP)	INOU OIL FAIICI

Pompe Disease (Glycogen Storage Disease Type II) (Glycogen and Lysosomal Storage Disorder)

Disease (common abbreviation)	Pompe Disease, Glycogen Storage Disease Type II (GSD II)
MIM #	232300
SNOMED Code / ICD-10-CM Coscidde	274864009 / E74.02
Enzyme or other abnormality	Acid alpha-glucosidase (GAA)
MIM # / Enzyme Commission #	606800 / 3.2.1.20
Abnormal Newborn Screening Metabolite(s)	Decreased GAA activity
LOINC Number(s)	63414-7
	Leukocyte GAA activity
Listial Diagnostics at Refound Courton	Mutation analysis of <i>GAA</i>
Initial Diagnostics at Referral Center	Determine cross-reactive immunologic material (CRIM) status
	Cardiac evaluation (echocardiogram (EKG))
Decommended additional testina to a 11	Serum creatine kinase (CK)
Recommended additional testing to consider	Urine glucose tetrasaccharide (Glc4)
at time of initial consultation	Alanine aminotransferase (ALT)
	Deficient GAA activity
Abu awa al Matabalitas Euroatad	Elevated CK
Abnormal Metabolites Expected	Elevated Glc4
	Elevated ALT
If initial testing is negative has the disorder been ruled out?	Yes
Diamondia Carifornia	Deficient GAA activity
Diagnostic Confirmation	Known pathological mutations in trans
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0017921%5BDISCUI
Genetic Testing Registry	%5D&condition=C0017921&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1261/
American College of Medical Genetics ACT	www.acmg.not/StatioContent/ACT/Pompa.ndf
Sheet	www.acmg.net/StaticContent/ACT/Pompe.pdf
American College of Medical Genetics	In development
Algorithm	in de velopment
Recommended Uniform Screening Panel	Core
(RUSP)	

### Krabbe Disease (Galactosylceramide Beta-Galactosidase Deficiency) (Other Genetic Condition)

(Othe	graduct Condition)
Disease (common abbreviation) MIM # SNOMED Code / ICD-10-CM Code Enzyme or other abnormality MIM # / Enzyme Commission #	Krabbe Disease; Galactosylceramide Beta-Galactosidase deficiency 245200 Not listed Galactosylceraminidase (GALC) 606890 / Not listed
Abnormal Newborn Screening Metabolite(s) LOINC Number(s)	Decreased GALC activity Mutation analysis in cases with low activity
Initial Diagnostics at Referral Center	Enzyme assay to Jefferson Lab Parents' and baby's blood spots to state for zygosity and mutation analysis Additional blood spot collected for HLA typing if needed
Recommended additional testing to consider at time of initial consultation	Not generally
Abnormal Metabolites Expected	Decreased enzyme activity Consistent mutation results
If initial testing is negative has the disorder been ruled out?	Yes (based on current experience)
Diagnostic Confirmation	Decreased enzyme activity Mutation analysis
Differential Diagnosis	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0023521%5BDISCUI %5D&condition=C0023521&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1238/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/Krabbe.pdf
American College of Medical Genetics Algorithm	In development
Recommended Uniform Screening Panel (RUSP)	Not on Panel

### Hurler Syndrome (Mucopolysaccharidosis, Type I), MPS I (Lysosomal Storage Disorder)

	mui storuge sisoruer)
Disease (common abbreviation)	Hurler Syndrome; Mucopolysaccharidosis, Type I (MPS I)
MIM #	607014
SNOMED Code / ICD-10-CM Code	7561003 / E76.01
Enzyme or other abnormality	α-L-iduronidase (IDUA)
MIM # / Enzyme Commission #	252800/3.2.1.76
Abnormal Newborn Screening Metabolite(s)	Deficient IDUA
LOINC Number(s)	55909-6
L'' ID' I D' I C	Repeat IDUA
Initial Diagnostics at Referral Center	Urine glucosaminoglycans (GAG)
Recommended additional testing to consider	
at time of initial consultation	Mutation analysis of IDUA
Abnormal Metabolites Expected	Increased heparin and dermatan sulfate (a GAG)
If initial testing is negative has the disorder	37
been ruled out?	Yes
Diagnostic Confirmation	Deficient IDUA
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0023786%5BDISCUI
Genetic Testing Registry	%5D&condition=C0023786&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1162/
American College of Medical Genetics ACT	No ACT sheet
Sheet	TWO THE I SHEET
American College of Medical Genetics	No algorithm
Algorithm	
Recommended Uniform Screening Panel	Not on panel
(RUSP)	

Hunter Syndrome (Mucopolysaccharidosis, Type II), MPS II (Lysosomal Storage Disorder)

Disease (common abbreviation)	Hunter Syndrome; Mucopolysaccharidosis, Type II (MPS II)
MIM #	309900
SNOMED Code / ICD-10-CM Code	70737009 / E76.1
Enzyme or other abnormality	Iduronate sulfatase (IDS)
MIM # / Enzyme Commission #	300823 / 3.1.6.13
Abnormal Newborn Screening Metabolite(s)	Deficient iduronate sulfatase activity
LOINC Number(s)	24087-9 (Enzymatic activity, serum)
Initial Diagnostics at Referral Center	Repeat iduronate sulfatase activity Urine GAG
Recommended additional testing to consider at time of initial consultation	Mutation analysis of IDS
Abu awa al Matabalitas Especial	Deficient iduronate sulfatase activity
Abnormal Metabolites Expected	Increased dermatan and heparan sulfate (GAG)
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Deficient iduronate sulfatase activity
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0026705%5BDISCUI
Genetic Testing Registry	%5D&condition=C0026705&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1274/
American College of Medical Genetics ACT Sheet	No ACT sheet
American College of Medical Genetics Algorithm	No algorithm
Recommended Uniform Screening Panel (RUSP)	Not on Panel

### Maroteaux-Lamy Syndrome (Mucopolysaccharidosis type VI), MPS VI (Lysosomal Storage Disorder)

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BDISCUI
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### X-Linked Adrenoleukodystrophy, X-ALD (Peroxisomal Disorder)

Disease (common abbreviation)	X-Linked Adrenoleukodystrophy (XALD)
Phenotype MIM #	300100
SNOMED Code / ICD-10-CM Code	1232670018 /
Enzyme or other abnormality	ATP-Binding Cassette
Gene MIM # / Enzyme Commission #	300371 /
Abnormal Newborn Screening Metabolite(s)	Very Long Chain Fatty Acid C26:0
LOINC Number(s)	ABCD1 mutation
Initial Diagnostics at Referral Center	Very Long-Chain Fatty Acid (Peroxisomal) Analysis Confirmatory mutation analysis
Recommended additional testing to consider	Plasmalogen analysis in patients with no identified mutation on
at time of initial consultation	newborn screening
Abnormal Metabolites Expected	Elevated C26:0, Elevated ratios C24:0/C22:0, C26:0/C22:0
	Pathological mutation in ABCD1 gene
If initial testing is negative has the disorder been ruled out?	Yes, but need to consider other peroxisomal disorders
Diagnostic Confirmation	Abnormal Mutation analysis of ABCD1 gene
Differential Diagnosis	Other Peroxisomal Disorders
Specific Testing Laboratories as listed in the	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=ABCD1&conditio
Genetic Testing Registry	<u>n=C0162309&amp;compare_labs=1</u>
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1315/
American College of Medical Genetics ACT Sheet	No ACT sheet
American College of Medical Genetics Algorithm	No algorithm
Recommended Uniform Screening Panel (RUSP)	No

#### Abbreviations

17-OHP 17-Hydroxyprogesterone

2,4Di 2,4-Dienoyl-CoA reductase deficiency

2M3HBA 2-Methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency

2MBG 2-Methylbutyryl glycinuria

3MCC 3-Methylcrotonyl-CoA carboxylase

3MGA 3-Methylglutaconic aciduria

A-Gal A Alpha-galactosidase A

ACTH Adrenocorticotrophic hormone

ADA Adenosine deaminase α-GalA Alpha-galactosodase A AFP Alpha fetoprotein AG Acylglycine

ALT Alanine aminotransferase

ARG Argininemia ARSB Arylsulfatase B

ASA Argininosuccinic aciduria ASM Acid sphingomyelinase B<sub>12</sub> Vitamin B<sub>12</sub>, cobalamin

BAER Brainstem auditory evoked response

BCKD Branched-chain alpha-keto acid dehydrogenase

BIOT Biotinidase deficiency, Biotinidase

βKT Beta-ketothiolase deficiency

C0 Free carnitine
C10 Decanoyl carnitine
C10:1 Decenoyl carnitine
C10:2 Decadienoyl carnitine
C14 Tetradecanoyl carnitine
C14:1 Tetradecenoyl carnitine
C16 Hexadecanoyl carnitine

C16OH Hydroxyhexadecanoyl carnitine

C18 Octadecanoyl carnitine C18:1 Octadecenoyl carnitine

C18:10H Hydroxyoctadecenoyl carnitine

C2 Acetyl-L-carnitine
C22:0 Docosanoic acid
C24:0 Tetracosanoic acid
C26:0 Hexacosanoic acid
C3 Propionyl carnitine
C3DC Malonyl carnitine

C4 Butyryl carnitine + isobutyryl carnitine

C4DC Methylmalonyl carnitine
C4OH Hydroxybutyryl carnitine
C5 Isovaleryl carnitine
C5:1 Tiglyl carnitine

C5DC Glutaryl carnitine

C5OH Hydroxyisovaleryl carnitine

C6 Hexanoyl carnitine
C6DC Methylglutaryl carnitine
C8 Octanoyl carnitine

CACT Carnitine-acyl carnitine translocase CAH Congenital adrenal hyperplasia

CBC Complete blood count
Cbl A,B Cobalamin A,B cofactor
Cbl C Cobalamin C cofactor
Cbl D<sub>1</sub> Cobalamin D<sub>1</sub> cofactor
Cbl D<sub>2</sub> Cobalamin D<sub>2</sub> cofactor
Cbl F Cobalamin F cofactor
Cbl J Cobalamin J cofactor

CBS Cystathionine beta-synthase

CF Cystic fibrosis

CFTR Cystic fibrosis transmembrane receptor

CH Congenital hypothyroidism

CIT I Citrullinemia type I
CIT II Citrullinemia type II
CK Creatine kinase

CPK Creatine phosphokinase

CPT I Carnitine palmitoyl transferase type I deficiency CPT II Carnitine palmitoyl transferase type II deficiency

CRIM Cross-reactive immunologic material

CSF Cerebrospinal fluid CUD Carnitine uptake defect EKG Electrocardiogram

EMA Ethylmalonic encephalopathy
FAH Fumarylacetoacetase hydrolase
FS Fetal and sickle cell hemoglobins
FSA Fetal, sickle and adult hemoglobins
FSC Fetal, sickle cell and C hemoglobins

GA 1 Glutaric acidemia type 1
GA 2 Glutaric acidemia type 2
GAA Acid alpha-glucosidase
GAG Glucosaminoglycans
Gal-1-P Galactose-1-phosphate
GALC Galactosylceraminidase

GALE Galactose epimerase deficiency

GALK Galactokinase

GALT Galactose-1-phosphate uriydltransferase

GD Gaucher disease

Glc4 Glucose tetrasaccharide

GLY Glycine

GSD II Glycogen storage disease, type II HADH Hydroxyacyl-CoA dehydrogenase

HbAS Sickle cell carrier (adult and sickle cell hemoglobins)

HbS Sickle cell hemoglobin

HbSB<sup>0</sup> Sickle cell beta zero thalassemia HbSB<sup>+</sup> Sickle cell beta plus thalassemia HbSC Sickle/hemoglobin C disease HCS Holocarboxylase synthetase

HCY Homocystinuria

HLA Human leukocyte antigen HMET Hypermethioninemia

HMG 3-Hydroxy-3-methylglutaryl-CoA lyase deficiency

H-PHE Hyperphenylalaninemia

HPLC High-performance liquid chromatography IBCD Isobutyryl-CoA dehydrogenase deficiency

IBG Isobutyrylglycinuria

ICD-10-CM International Classification of Diseases, 10<sup>th</sup> Revision, Clinical Modification

IDS Iduronate sulfatase
IDUA Alpha-L-iduronidase
IEM Inborn error of metabolism

ILE Isoleucine

IRT Immunoreactive trypsinogen

IVA Isovaleric acidemia

K Potassium

LCHAD Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

LOINC Logical Observation Identifiers Names and Codes

MA Malonic aciduria

MADD Multiple acyl-CoA dehydrogenase deficiency

MAT Methionine adenesyltransferase

MCAD Medium-chain acyl-CoA dehydrogenase deficiency

MCD Multiple carboxylase deficiency

MCKAT Medium-chain ketoacyl-CoA thiolase deficiency

MET Methionine

MHBD 2-Methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency

MIM Mendelian Inheritance in Man MLYCD Malonyl-CoA decarboxylase

MMA Methylmalonic acid

MPS I Mucopolysaccharidosis, type I, Hurler syndrome MPS II Mucopolysaccharidosis, type II, Hunter syndrome

MPS IV Mucopolysaccharidosis, type IV, Maroteaux-Lamy syndrome

MRI Magnetic resonance imaging

M/SHAD Medium/short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency

MSUD Maple syrup urine disease

MUT Methylmalonic-CoA mutase deficiency

NA Sodium
N/A Not available
NK Natural killer cells

OCTN2 Organic cation/carnitine transporter

OH Hydroxy

PA Propionic acidemia
PAA Plasma amino acids
PHE Phenylalanine
PKU Phenylketonuria
RBC Red blood cell

RUSP Recommended Universal Screening Panel

SA Succinylacetone

SAA Succinylacetoacetate

SAH S-adenosyl homocysteine hydrolase

SCAD Short-chain acyl-CoA dehydrogenase deficiency

SCHAD Short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency

SCID Severe combined immunodeficiency SNOMED Systematized Nomenclature of Medicine

SS Sickle cell anemia

SUCLA<sub>1</sub> Succinate-CoA lyase, alpha subunit SUCLA<sub>2</sub> Succinate-CoA lyase, beta subunit SUM AC Sum of all acylcarnitine levels

T3 Triiodothyronine

T4 Thyroxine

TFP Trifunctional protein deficiency
TREC T-cell receptor excision circle
TPN Total parenteral nutrition
TSH Thyroid stimulating hormone

TTN Transient tyrosinemia of the newborn

TYR Tyrosine

TYR I Tyrosinemia type I
TYR II Tyrosinemia type II
TYR III Tyrosinemia type III
UAG Urine acylglycine
UOA Urine organic acids

VAL Valine

VLCAD Very long-chain acyl-CoA dehydrogenase deficiency

X-ALD X-Linked Adrenoleukodystrophy