

New York Mid-Atlantic Caribbean Regional Genetics Network

Delaware, District of Columbia, Maryland, New Jersey, New York, Pennsylvania, Puerto Rico, US Virgin Islands, Virginia, West Virginia

Diagnostic Guidelines for Confirmation of Screen-Positive Newborn Screening Results

Updated: September 2014

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Table of Contents

Abbreviations	68
Acid Sphingomyelinase (ASM) Deficiency	60
Adrenal Hyperplasia, Congenital (CAH)	4
Amino Acidemias	9-19
Argininemia (ARG)	
Argininosuccinic Aciduria (ASA) - aka Argininosuccinic Lyase Deficiency	10
Argininosuccinic Lyase Deficiency - aka Argininosuccinic Aciduria (ASA)	10
Beta-Ketothiolase Deficiency (BKT) - aka Beta-Oxothiolase Deficiency	44
Beta-Oxothiolase Deficiency - aka Beta-Ketothiolase Deficiency (BKT)	44
Biotinidase Deficiency (BIOT)	53
Carnitine-Acylcarnitine Translocase Deficiency (CACT)	
Carnitine Palmitoyl Transferase Type Ia Deficiency (CPT-Ia)	
Carnitine Palmitoyl Transferase Type II Deficiency (CPT-II)	21
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	12
Classical Galactosemia (GALT)	
Cobalamin A,B Cofactor (Cbl A/B)	
Cobalamin C Cofactor Deficiency (Cbl C)	
Cobalamin D ₁ Cofactor Deficiency (Cbl D ₁)	
Cobalamin D ₂ Cofactor Deficiency (Cbl D ₂)	
Cobalamin F Cofactor Deficiency (Cbl F)	
Cobalamin J Cofactor Deficiency (Cbl J)	
Congenital Adrenal Hyperplasia (CAH)	
Congenital Hypothyroidism (CH)	
Cystic Fibrosis (CF)	
2,4-Dienoyl-CoA Reductase Deficiency (2,4Di)	
Endocrinopathies	
Ethylmalonic Encephalopathy (EMA)	
Fabry Disease	
Fatty Acid Oxidation Disorders	
Galactose Epimerase Deficiency (GALE)	
Galactokinase Deficiency (GALK)	
Galactosemia (Classical) (GALT)	
Galactosylceramide Beta-Galactosidase Deficiency	
Gaucher Disease (GD)	
Glucocerebrosidase Deficiency	
Glucosylceramidase Deficiency, not including Saposin C Deficiency	
Glutaric Acidemia Type I (GA-I)	
Glutaric Acidemia Type II (GA-II)	
Glycogen Storage Disease Type II (GSD II)	
Hemoglobin S/Beta ⁰ Thalassemia (HbS ⁰)	
Hemoglobin S/Beta ⁺ Thalassemia (HbS ⁺)	
Hemoglobin SS (SS)	
Hemoglobinopathies	
Hemoglobinopathies, Other	
Homocystinuria (HCY)	
Hunter Syndrome	65

Hurler Syndrome	
3-@Hydroxyacyl-Co-A Dehydrogenase Deficiency (HADH)	30
4-Hydroxyphenylpyruvic Acid Oxidase Deficiency	19
3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG)	46
Hypermethioninemia (MET)	14
Hyperphenylalaninemia (H-PHE)	16
Hypothyroidism, Primary Congenital (CH)	5
Hypothyroidism, Secondary Congenital	5
Isobutyryl-CoA Dehydrogenase Deficiency (IBCD)	35
Isobutyrylgylcinuria (IBG)	
Isovaleric Acidemia (IVA)	
Krabbe Disease	
Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)	25
Lysosomal Storage Disorders	
Malonic Aciduria (MAL)	
Maple Syrup Urine Disease (MSUD)	
Maroteaux-Lamy Syndrome (MPS VI)	
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)	
Methylmalonic Acidurias	
Methylmalonyl-CoA Mutase Deficiency (MUT)	
Mucopolysaccharidosis Type I (MPS I)	
Mucopolysaccharidosis Type II (MPS II)	
, ,	
Mucopolysaccharidosis Type VI (MPS VI)	
Multiple Carboxylase Deficiency (MCD)	
Niemann-Pick Syndrome, Types A, B	
Organic Acidemias	
Other Hemoglobinopathies	
Phenylketonuria (PKU)	
Pompe Disease	
Primary Carnitine Deficiency	
Primary Congenital Hypothyroidism (CH)	
Propionic Acidemia (PA)	
S-Adenosylhomocysteine Hydroxolase (SAH)	
Secondary Congenital Hypothyroidism	
Severe Combined Immune Deficiency (SCID)	
Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD)	
Sickle Cell Carrier (HbAS)	
Sickle Cell Disease	
Sickle C Disease (HbSC)	
T-cell-related Lymphocyte Deficiencies	
Thyroxine-Binding Globulin Deficiency	5

Trifunctional Protein Deficiency (TFP)	. 31
Tyrosinemia Type I (TYR-I)	. 17
Tyrosinemia Type II (TYR-II)	. 18
Tyrosinemia Type III (TYR-III)	
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	
X-Linked Adrenoleukodystrophy (X-ALD)	. 67

Congenital Adrenal Hyperplasia (CAH) (Endocrine Disorder)

	Indocrine 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
	ACTH stimulation test
	Mutation analysis
	Severe:
	Markedly elevated 17-OHP
Abnormal Metabolites Expected	Decreased sodium, increased potassium, low glucose
	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 170HP.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

^{**} 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⁺ Thalassemia (HbSB⁺), Hemoglobin S/Beta⁰ Thalassemia (HbSB⁰),

and Sickle C Disease (HbSC)

(Hemoglobinopathy)

Disease (common abbreviation)	Sickle Cell Disease including Hemoglobin SS (SS), Hemoglobin
	S/Beta ⁺ Thalassemia (HbSß ⁺), Hemoglobin S/Beta ⁰
	Thalassemia (HbSß ⁰) 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 at time of initial consultation	CBC
	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?	165
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
	HbSß ^O , HbSß ⁺ :
Specific Testing Laboratories as listed in	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0221019%5BDISCUI%
Genetic 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, HbSß ⁰ :
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/ACT_sheet_HBSS_FS 4.28.
	<u>06%20ljo.pdf</u>
	HbSß ⁺ : www.acmg.net/StaticContent/ACT/ACT-
	sheet Hb Sbeta plus thal FSA.pdf
	HbSC: www.acmg.net/StaticContent/ACT/ACT-
	sheet HBSC FSC.pdf

Algorithm	wwww.acmg.net/StaticContent/ACT/Algorithms/Visio- Hemoglobinopathy 4.18.06.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Other Hemoglobinopathies (Hemoglobinopathy)

Disease (common abbreviation)	Other Hemoglobinopathies
,	141900
MIM#	
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. 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 Algorithm	All Hemoglobinopathies:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
7.195775	Hemoglobinopathy 4.18.06.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Sickle Cell Carrier (HbAS) (Hemoglobinopathy)

,	
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	CBC
Abnormal Metabolites Expected	FAS
Abnormal Metabolites Expected	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 trait
Sheet	FAS.pdf
American College of Medical Genetics Algorithm	All Hemoglobinopathies:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Hemoglobinopathy 4.18.06.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Argininemia (ARG) (Amino Acidemias)

V.	Arimo 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)	Elevated arginine
LOINC Number	47562-4
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
Pacammandad additional tacting to consider	Liver function tests
Recommended additional testing to consider 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
Abnormal Metabolites Expected	Normal/slightly elevated ammonia
	Normal/elevated orotic acid
If initial testing is negative has the disorder	Yes
been ruled out?	Tes .
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	www.acmg.not/StaticContent/ACT/Argining.ndf
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 (RUSP)	Secondary Target

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

	,
Disease (common abbreviation)	Argininosuccinic Lyase Deficiency; Argininosuccinic Aciduria
	(ASA)
MIM #	207900
SNOMED Code / ICD-10-CM Code	41013004 / E72.22
Enzyme or other abnormality	Argininosuccinic lyase
MIM # / Enzyme Commission #	608310 / 4.3.2.1
Abnormal Newborn Screening Metabolite(s)	Elevated citrulline (some states elevated ASA)
LOINC Number(s)	42892-0
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
Initial Diagnostics at Rejerral Center	Urine orotic acid
Recommended additional testing to consider	Liver function tests
at time of initial consultation	Ammonia
	Elevated citrulline, glutamine, and argininosuccinic acid (PAA)
	Decreased arginine (PAA)
Abnormal Metabolites Expected	Elevated urine orotic acid possible
	Normal liver function tests expected
	Elevated ammonia expected
If initial testing is negative has the disorder	Yes
been ruled out?	les
Diagnostic Confirmation	Elevated argininosuccinic acid
Differential Diagnosis	Citrullinemia Type I (CIT I); Citrullinemia Type II (CIT II)/Citrin Deficiency
Specific Testing Laboratories as listed in	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268547%5BDISCUI%
Genetic Testing Registry	5D&condition=C0268547&compare labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK51784/
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)	Core Panel

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

	(Affilio Acideffia)	
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	
110.	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	V	
been ruled out?	Yes	
	Elevated citrulline, (and alanine and glutamine if sick) and orotic	
	acid levels	
Diagnostic Confirmation	Enzyme analysis in fibroblasts	
	Mutation analysis is required to differentiate between mild CIT	
	Type I and Citrin Deficiency	
Differential Diggraphic	Argininosuccinic Lyase Deficiency/ Argininosuccinic Aciduria	
Differential Diagnosis	(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	
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1458/	
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	Core Panel	
(RUSP)		

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

	7 Time / Gracima,
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
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
mitial biagnostics at Negerial 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)
Abnormal Metabolites Expected	Elevated urine orotic acid possible
Abhornial Wetabolites 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?	TES .
	Elevated citrulline with normal ammonia and glutamine levels
Diagnostic Confirmation	Mutation analysis is required to differentiate between mild CIT
	Type I and Citrin Deficiency
Differential Diagnosis	Argininosuccinic Lyase Deficiency/ Argininosuccinic Aciduria
Dijjerentiai 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
(/	I

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

Homocystinuria (HCY) (Amino Acidemia)

•
Homocystinuria (HCY)
236200
24308003 / E72.11
Cystathionine beta-synthase (CBS)
236300 / 4.2.1.22
Elevated methionine
47700-0
Plasma amino acids (PAA)
Total plasma homocysteine
Urine organic acids (UOA)
Liver function tests
Elevated methionine, free homocystine and total homocysteine
(PAA)
No succinylacetone (UOA)
Normal liver function tests expected
Yes
res
Elevated methionine, free homocystine and total homocysteine
Evaluate for B6 responsiveness and/or do mutation analysis
Hypermethioninemia (HMET)/Tyrosinemia Type I (TYR I)/Liver Disease
www.ncbi.nlm.nih.gov/gtr/tests/?term=C3150344%5BDISCUI%
5D&condition=C3150344&compare labs=1
www.ncbi.nlm.nih.gov/books/NBK1524/
www.acmg.not/StatisContant/ACT/Mathianing.ndf
www.acmg.net/StaticContent/ACT/Methionine.pdf
www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Methionine.pdf
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	www.acmg.net/staticcontent/ACT/Metinonine.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Methionine.pdf
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
	Elevated leucine + isoleucine
Abnormal Newborn Screening Metabolite(s)	
LOINC Number(s)	53152-5
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
	Urine organic acids (UOA)
Recommended additional testing to consider	Urine ketones
at time of initial consultation	
	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	Vec
been ruled out?	Yes
	Elevated branched-chain amino acids and elevated
	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	
Sheet	www.acmg.net/StaticContent/ACT/Leucine.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Leucine.pdf
Recommended Uniform Screening Panel	<u>Leadine.pai</u>
,	Core Panel
(RUSP)	

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 been ruled out?	Yes
Diagnostic Confirmation	Elevated phenylalanine levels
Differential Diagnosis	Defects of Biopterin Metabolism, Neonates on Total Parenteral 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 Sheet	www.acmg.net/StaticContent/ACT/Phenylalanine.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	<u>Phenylalanine.pdf</u>
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

	Amino Acidemia)
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
Abnormal Newborn Screening Metabolite(s)	first screen)
LOINC Number(s)	35571-9
Lenve Manneer(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 at time of initial consultation	Alpha fetoprotein
	Elevated tyrosine, methionine (PAA)
Ab 0.4 - + - -	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
Differential Diagnosis	Tyrosinemia Type II (TYR II); Tyrosinemia Type III (TYR III), 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 Genetic Testing Registry	
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1515/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/Tyrosine.pdf
American College of Medical Genetics Algorithm	Tyrosine normal/elevated; succinylacetone elevated: www.acmg.net/StaticContent/ACT/Algorithms/Visio- Tyrosine normal or elevated and SUAC elevated DM.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

	Amino Acidemia)
Disease (common abbreviation)	Tyrosinemia Type II (TYR-II)
MIM #	276600
SNOMED Code / ICD-10-CM Code	4887000 / E70.21
Enzyme or other abnormality	Tyrosine aminotransferase
MIM # / Enzyme Commission #	613018 / 2.6.1.5
	Elevated tyrosine
Abnormal Newborn Screening Metabolite(s)	35571-9
LOINC Number(s)	Normal 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	Alaba fatanastain
at time of initial consultation	Alpha fetoprotein
	Elevated tyrosine (PAA)
	Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-
	tyramine, N-acetyltyrosine (UOA)
Abnormal Metabolites Expected	Normal succinylacetone (UOA)
	Normal liver function tests expected
	Normal alpha fetoprotein (after neonatal period)
If initial testing is negative has the disorder	W
been ruled out?	Yes
	Persistence of tyrosine elevation, with negative succinylacetone
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
Differential Diagnosis	Parenteral Nutrition (TPN), Transient Tyrosinemia of the
3	Newborn
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268487%5BDISCUI%
Genetic Testing Registry	5D&condition=C0268487&compare labs=1
Specific Testing Laboratories as listed in the	
Genetic Testing Registry	
GeneReviews	None
American College of Medical Genetics ACT	
Sheet	www.acmg.net/StaticContent/ACT/Tyrosine.pdf
	Tyrosine elevated; succinylacetone normal:
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Tyrosine elevated, SUAC normal.pdf
Recommended Uniform Screening Panel	
(RUSP)	Secondary Target
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Tyrosinemia Type III (TYR-III); 4-Hydroxyphenylpyruvic Acid Oxidase Deficiency (Amino Acidemia)

	Amino Acidemia)
Disease (common abbreviation)	Tyrosinemia Type III (TYR-III); 4-Hydroxyphenylpyruvic Acid
MIM #	Oxidase Deficiency
SNOMED Code / ICD-10-CM Code	276710
Enzyme or other abnormality	415764005 / E70.21
	4-Hydroxyphenylpyruvic acid oxidase
MIM # / Enzyme Commission #	276710 / 1.13.11.27
	Elevated tyrosine
Abnormal Newborn Screening Metabolite(s)	35571-9
LOINC Number(s)	Normal 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	Alula fata unatain
at time of initial consultation	Alpha fetoprotein
	Elevated tyrosine (PAA)
	Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-
Ab.,	tyramine, N-acetyltyrosine (UOA)
Abnormal Metabolites Expected	Normal succinylacetone (UOA)
	Normal liver function tests expected
	Normal alpha fetoprotein (after neonatal period)
If initial testing is negative has the disorder	Yes
been ruled out?	les
	Persistence of tyrosine elevation, with negative succinylacetone
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
Differential Diagnosis	Parenteral Nutrition (TPN), Transient Tyrosinemia of the
	Newborn
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268623%5BDISCUI%
Genetic Testing Registry	5D&condition=C0268623&compare labs=1
Specific Testing Laboratories as listed in the	
Genetic Testing Registry	
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/Tyrosine.pdf
Sheet	Tyrasina alayatad, susainylasatana namasi.
American College of Medical Genetics	Tyrosine elevated; succinylacetone normal:
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Tyrosine elevated, SUAC normal.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

Carnitine Palmitoyl Transferase Type Ia Deficiency (CPT-Ia)

(Fatty Acid Oxidation Disorder)

Diagram (agreement white the transfer of the t	Compiting Delmitary Transferage Time 1- Deficiency (CDT 1)
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 la
MIM # / Enzyme Commission #	600528 / 2.3.1.21
	Elevated CO
Abnormal Newborn Screening Metabolite(s)	38481-8
LOINC Number(s)	Elevated CO/(C16+C18) ratio*
	53235-8
	Carnitine, total and free in blood spot (<1 wk)
1 1.	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
	Elevated CO/(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	Gracose revers depend on red status or patient
been ruled out?	Yes
Deell Tuleu out:	* If initial CO/(C16+C18) ratio >100 or if expected abnormal
	metabolites are seen (Blood spot ratios valid in infants less
Diagnostic Confirmation	l · · · · · · · · · · · · · · · · · · ·
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	1/01 1/ C 1 1/ACT/CO 01/C 01/O 1/
Sheet	www.acmg.net/StaticContent/ACT/C0 C16-C18.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	C0.vsd; C0.vsd;C16-C18.pdf
Recommended Uniform Screening Panel	Casandamy Tayrat
(RUSP)	Secondary Target
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Carnitine Palmitoyl Transferase Type II Deficiency (CPT-II) (Fatty Acid Oxidation Disorder)

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

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

Disease (common abbreviation) MIM #	Carnitine-Acylcarnitine Translocase Deficiency (CACT) 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
William Ferragine Commission in	Elevated C16
Abnormal Newborn Screening Metabolite(s)	53199-6
LOINC Number(s)	Elevated C18:1
	53202-8
133 103 13 10 10 1	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
Abnormal Metabolites Expected	Elevated C16, C18:1
Abhornar Wetabolites Expected	CPK may 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
Diagnostic Confirmation	Mutation analysis with detection of two known or likely
Diagnostic Conjunitation	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	
Genetic Testing Registry	
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C16 and-or C18-1.pdf
Sheet	
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C16 and-
Algorithm	or C18.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

Carnitine Uptake Defect (CUD); Primary Carnitine Deficiency (Fatty Acid 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 CO
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
	Urine Carnitine, total and free
Recommended additional testing to consider	Creatinine phosphokinase (CPK)
at time of initial consultation	Blood glucose
	Decreased carnitine, total and free
	Decreased acylcarnitines (long-chain)
	Elevated total and free urine carnitine
Abnormal Metabolites Expected	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	Vec (are sided as equalities of an less estation)
been ruled out?	Yes (provided no carnitine supplementation)
	Enzyme assay (OCTN2) in fibroblasts and/or mutation analysis if
Diagnostic Confirmation	functional assay unclear
	Consider maternal testing
	Consider other non-genetic causes of carnitine deficiency –
Differential Diagnosis	nutritional, renal insufficiency, other primary IEMs and
	maternal CUD or IEMs
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342788%5BDISCUI%
Genetic Testing Registry	5D&condition=C0342788&compare labs=1
Specific Testing Laboratories as listed in the	
Genetic Testing Registry	
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK84551/
American College of Medical Genetics ACT	www.acma.not/StaticContont/ACT/CO.ndf
Sheet	www.acmg.net/StaticContent/ACT/C0.pdf
American College of Medical Genetics	www.acma.not/StaticContent/ACT/Algorithms/A/isia.CO.ndf
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C0.pdf
Recommended Uniform Screening Panel	Core Panel
(RUSP)	Core i anei

2,4-Dienoyl-CoA Reductase Deficiency (2,4Di)

(Fatty Acid Oxidation Disorder)

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
•	222745 / 1.3.1.34
MIM # / Enzyme Commission #	·
Abnormal Newborn Screening Metabolite(s)	Elevated C10:2
LOINC Number(s)	53180-64
Initial Diagnostics at Referral Center	Acylcarnitine profile
miliar biagnostics at negeriar 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	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=dienoyl-coa
Genetic Testing Registry	reductase&condition=CN037048&compare labs=1
GeneReviews	None
American College of Medical Genetics ACT	No ACT sheet
Sheet	IND ACT SHEEL
American College of Medical Genetics	NI I
Algorithm	No algorithm
Recommended Uniform Screening Panel (RUSP)	Secondary Target

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

Disease (common abbreviation)	Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency
A 41A 4 H	(LCHAD)
MIM#	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
Ab N C N - + - !+ - / -	Elevated C16OH
Abnormal Newborn Screening Metabolite(s)	50125-4
LOINC Number(s)	Elevated C18:10H
	50113-0
	Acylcarnitine profile
Initial Diagnostics at Referral Center	Urine organic acids
,	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)
Bragnostic conjirmation	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	<u>I]&condition=CN074230&compare labs=1</u>
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C16-OH.pdf

American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C16-OH +- -C18-1-OH.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

Disease (common abbreviation)	Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
MIM#	201450
SNOMED Code / ICD-10-CM Code	128596003 / E71.311
Enzyme or other abnormality	Medium-chain acyl-CoA dehydrogenase
MIM # / Enzyme Commission #	607008 / 1.3.99.3
	Elevated C8
Abnormal Newborn Screening Metabolite(s)	53175-6
LOINC Number(s)	Lesser elevation of C6 and C10, C10:1
,	45211-0, 45197-1, 45198-9
	Mutation detection in some states
Initial Diagnostics at Referral Center	Acylcarnitine profile and
3	Urine organic acids and/or urine acylglycines
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Plasma Carnitine, total and free
,	
	Elevated C6, C8, C10 (acylcarnitines)
	C6 <c8>C10</c8>
	Elevated hexanoylglycine and suberylglycine (acylglycines)
Abnormal Metabolites Expected	Blood glucose depends on fed status of patient
	Normal/Low plasma carnitine levels
	Elevated dicarboxylic acids, especially suberic acid, with no
	excess ketones (UOA)
If initial testing is negative has the disorder	Yes
been ruled out?	
	Typical pattern of acylcarnitines is diagnostic - C6 <c8>C10</c8>
Diagnostic Confirmation	Elevated urine hexanoglycine and suberylglycine
	Mutation analysis widely available
	Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT);
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=C0220710%5BDISCUI%
Genetic Testing Registry	5D&condition=C0220710&compare labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1424/
American College of Medical Genetics ACT	
Sheet	www.acmg.net/StaticContent/ACT/C8 C6 C10.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	C8.vsd; C6-C10.pdf
Recommended Uniform Screening Panel	Carra Daniel
(RUSP)	Core Panel

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

	Cid Oxidation Bisorder/
Disease (common abbreviation)	Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT)
MIM #	602199
SNOMED Code / ICD-10-CM Code	124265004 / None
Enzyme or other abnormality	Medium-chain ketoacyl-CoA thiolase
MIM # / Enzyme Commission #	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 Negerial Center	Urine organic acids
	Blood glucose
Recommended additional testing to consider	Urine ketones
at time of initial consultation	Plasma Carnitine, total and free
at 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 been ruled out?	Unknown
Diagnostic Confirmation	No specific recommendations
-166	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 Sheet	No ACT Sheet
American College of Medical Genetics	
Algorithm	No Algorithm
Recommended Uniform Screening Panel (RUSP)	Secondary Target
(NOSI)	

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

Disease (common abbreviation)	Multiple Acyl-CoA Dehydrogenase Deficiency (MADD); Glutaric
	Acidemia Type II (GA-II)
MIM#	231680
SNOMED Code / ICD-10-CM Code	22886006 / E71.313
Enzyme or other abnormality	Electron Transfer Flavoprotein (alpha, beta subunit)
MIM # / Enzyme Commission #	608053, 130410, 231675 / 1.5.5.1
Abnormal Newborn Screening Metabolite(s)	Elevated C4, C5, C6, C8, C10
LOINC Number(s)	53166-5, 45216-9, 45211-0, 53175-6, 45197-1
	Acylcarnitine profile
Initial Diagnostics at Referral Center	Urine organic acids
	Urine acylglycines
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Creatinine phosphokinase (CPK)
at time of initial consultation	Liver function tests
	Elevated C4, C5, C6, C8, C10 and long-chain acylcarnitines
	Elevated lactate, 2-OH-glutarate, ethylmalonic acid and adipic
	acids (UOA)
Abnormal Metabolites Expected	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
If initial testing is negative has the disorder	Yes
been ruled out?	
	Abnormal metabolite pattern is diagnostic
	If not found, need
	1) Mutation analysis with two known or likely pathological
Diagnostic Confirmation	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);
Differential Diagnosis	Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT),
	Mitochondrial Disorder, Riboflavin Deficiency, Maternal
	Disorder
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268596%5BDISCUI%
Genetic Testing Registry	5D&condition=C0268596&compare labs=1
GeneReviews	None
American College of Medical Genetics ACT	A CT/CA CE II
Sheet	www.acmg.net/StaticContent/ACT/C4 C5.pdf

American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4 C5 + other AC.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

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

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 Diagnostics at Referral Center	Plasma acylcarnitine profile
Initial Diagnostics at Rejerral 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	Yes
been ruled out?	TES .
Diagnostic Confirmation	Mutation analysis with 2 known or likely pathological mutations in trans
	Ethylmalonic Encephalopathy (EMA); Isobutyryl-CoA
Differential Diagnosis	Dehydrogenase Deficiency (IBCD); presence of SCAD
	polymorphisms
Specific Testing Laboratories as listed in the	www.nchi.nlm.nih.gov/gtr/tosts/2torm-short.chain.cov/1.coa
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.not/StaticContont/ACT/CA.ndf
Sheet	www.acmg.net/StaticContent/ACT/C4.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4.pdf
Algorithm	www.acmg.ner/staticcontent/Act/Aigontinns/visio-c4.put
Recommended Uniform Screening Panel (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
A 41A 4 1/	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
Ab	Elevated/normal ketone bodies on urine organic analysis
Abnormal Metabolites 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
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
Specific Testing Laboratories as listed in the	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
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4-OH.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

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

Disease (common abbreviation)	Trifunctional Protein Deficiency (TFP)
MIM #	609015
SNOMED Code / ICD-10-CM Code	237999008 / E88.39
Enzyme or other abnormality	Trifunctional protein (alpha, beta subunit)
MIM # / Enzyme Commission #	600890, 143450 / 1.1.1.211
IVIIIVI # / EIIZYIIIE COIIIIIIISSIOII #	Elevated C16OH
Abnormal Nowborn Carooning Matabalita(s)	50125-4
Abnormal Newborn Screening Metabolite(s)	Elevated C18:10H
LOINC Number(s)	50113-0
	Acylcarnitine profile
Initial Diagnostics at Referral Center	Urine organic acids
	Mutation analysis, as negative metabolites do not rule out the
	disorder
Description and additional trations to a sile	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, C18:10H (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 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
If initial testing is negative has the disorder	Yes
been ruled out?	
	Mutation analysis for combined LCHAD/TFP:
	0 mutation – disease unlikely (unless consanguineous and as
	long as metabolites normal)
Diagnostic Confirmation	1 known or likely pathological mutation - proceed to enzyme
	assay or functional (probe) study
	2 known or likely pathological mutations in trans – diagnosis
	confirmed
Differential Diagnosis	Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency
Dijjerentiai Diagnosis	(LCHAD)
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342786%5BDISCUI%
Genetic Testing Registry	5D&condition=C0342786&compare labs=1
GeneReviews	None
American College of Medical Genetics ACT	
Sheet	www.acmg.net/StaticContent/ACT/C16-OH.pdf
	1

American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C16-OH +- -C18-1-OH.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

Disease (common abbreviation) MIM # SNOMED Code / ICD-10-CM Code Enzyme or other abnormality MIM # / Enzyme Commission #	Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD) 201475 237997005 / E71.310 Very long-chain acyl-CoA dehydrogenase 609575 / 1.3.99.13
Abnormal Newborn Screening Metabolite(s) LOINC Number(s)	Elevated C14 53192-1 Elevated C14:1 53191-3
Initial Diagnostics at Referral Center	Plasma acylcarnitine profile Mutation analysis, as negative metabolites do not rule out the disorder
Recommended additional testing to consider at time of initial consultation	Blood glucose Plasma Carnitine, total and free Creatinine phosphokinase (CPK) Urine organic acids Liver function tests
Abnormal Metabolites Expected	Elevated C14, C14:1 Detection of known pathological mutations in trans Blood glucose depends on fed status of patient Normal/low carnitine levels CPK may be elevated in sick patients Urine organic acids are usually normal Liver function tests may be abnormal in sick patients
If initial testing is negative has the disorder been ruled out?	No
Diagnostic Confirmation	Mutation analysis: 0 mutation disease unlikely (unless consanguineous, and as long as metabolites are normal) 1 mutation - proceed to enzyme assay or functional probe 2 known or likely pathological mutations in trans confirms diagnosis
Differential Diagnosis	Carnitine Palmitoyl Transferase Type II Deficiency (CPT II), 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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342784%5BDISCUI% 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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C14- 1 DM.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Ethylmalonic Encephalopathy (EMA) (Fatty Acid 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
The state of the s	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)
Initial Diagnostics at Referral Center	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
	Elevated ethylmalonic acid, methylsuccinic acid and lactate (UOA)
Abnormal Metabolites Expected	Elevated C4 in plasma and urine
The man metabolites Expected	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 been ruled out?	Yes
Diagnostic Confirmation	Abnormal metabolite pattern with clinical phenotype Mutation analysis with two known or likely pathological
Diagnostic confirmation	mutations in trans (may not be available in US)
Differential Diagnosis	Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD);
,,	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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4.pdf
Recommended Uniform Screening Panel (RUSP)	Not on Panel

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

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
Initial Diagnostics at Referral Center	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	Vac
been ruled out?	Yes
Discourantia Carofinanatia a	Abnormal metabolite pattern, and mutation analysis with two
Diagnostic Confirmation	known or likely pathological mutations in trans
D:((): 10: :	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.not/StaticContent/ACT/C4.ndf
Sheet	www.acmg.net/StaticContent/ACT/C4.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C4.pdf
Algorithm	www.acmg.net/staticeontent/ACT/Aigontinns/visio-c4.put
Recommended Uniform Screening Panel	Secondary Target
(RUSP)	Secondary ranget

Methylmalonic Acidemia - Cobalamin A,B Cofactor Deficiency (Cbl A,B); Cobalamin D₁ Cofactor Deficiency (CblD₁)

(Organic Acidemia)

Disease (common abbreviation)	Methylmalonic Aciduria - Cobalamin A,B Cofactor (Cbl A,B);
	Cobalamin D ₁ Cofactor Deficiency (Cbl D ₁)
MIM # SNOMED Code / ICD-10-CM Code Enzyme or other abnormality MIM #	251100 (A), 251110 (B)
	73843004 (A), 82245003 (B) / E71.120
	Cobalamin A,B cofactor deficiency
	607481 (A), 607568 (B)
/ Enzyme Commission #	Cobalamin D ₁ cofactor
/ Litzyine 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
Initial Diagnostics at Referral Center	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
at time of initial consultation	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 ₁₂ levels
Abhormarivietabolites 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	Yes
been ruled out?	
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 ₂ Cofactor Deficiency (Cbl D ₂); Methylmalonic-CoA Mutase Deficiency (MUT); Propionic Acidemia (PA); Succinate-CoA Ligase, beta subunit (SUCLA ₂); Succinate-CoA Ligase, alpha subunit (SUCLG ₁)
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 D₂ Cofactor Deficiency (Cbl D₂), Cobalamin F Cofactor Deficiency (Cbl F); Cobalamin J Cofactor Deficiency (Cbl J)

(Organic Acidemia)

Disease (common abbreviation)	Methylmalonic Aciduria - Cobalamin C Cofactor Deficiency (Cbl
	C); Cobalamin D ₂ Cofactor Deficiency (Cbl D ₂); 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 ₂ 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
	Elevated C3
Abnormal Newborn Screening Metabolite(s)	53160-8
LOINC Number(s)	Elevated C4DC
· ·	45222-7 (?low methionine in some states)
	Urine organic acids (UOA)
	Plasma acylcarnitine profile
110.	Plasma methylmalonic acid (MMA)
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
	Total homocysteine
	B12 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 total homocysteine
	Elevated MMA (UOA)
	Normal amino acids (may have elevated free homocystine and
	low methionine) (PAA)
Abnormal Metabolites Expected	Normal/elevated B ₁₂ levels
	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	Yes
been ruled out?	103

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. Complementation studies in fibroblasts
Differential Diagnosis	Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D_1 Cofactor Deficiency (Cbl D_1); 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 ₂ : 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
	Ammonia
	Elevated 3-OH-isovaleric acid, lactate, tiglylglycine, 3-
	methylcrotonylglycine, methylcitrate, 3-OH propionate (UOA)
	Elevated C5OH and C3 (plasma acylcarnitines)
Abnormal Metabolites 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 been ruled out?	Yes
	Mutation analysis:
	0 mutation - disease unlikely (unless consanguineous)
Diagnostic Confirmation	1 mutation - proceed to enzyme assay
Diagnostic Confirmation	2 known or likely pathological mutations in trans confirms
	diagnosis
	Enzyme analysis in fibroblasts and lymphocytes
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-OH.pdf
Algorithm	
Recommended Uniform Screening Panel	Core Panel
(RUSP)	

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

	Mathylpselepul Co A Mutaga Dafiaianay (NAUT)
Disease (common abbreviation)	Methylmalonyl-CoA Mutase Deficiency (MUT)
MIM#	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 Diagnostics at Referral Center	Plasma methylmalonic acid
	Plasma amino acids (PAA)
	Total homocysteine
	B ₁₂ levels in patient and mother
	Electrolytes (especially if sick)
Recommended additional testing to consider	Blood glucose
at time of initial consultation	Ammonia
at time of mitial consultation	Carnitine, total and free
	Urine ketones
	Elevated methylmalonic acid (UOA and in plasma)
	Elevated 3-OH-propionic acid, methylcitric acid, (UOA)
	Elevated glycine (PAA)
	Normal homocysteine and B ₁₂ 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	V
been ruled out?	Yes
	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
	Complementation studies in fibroblasts
	Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D ₁ Variant (Cbl
D:((): 10:	D ₁); Cobalamin C Cofactor Deficiency (Cbl C) (normal or
Differential Diagnosis	increased homocysteine); Cobalamin D ₂ Cofactor Deficiency
	(Cbl D ₂) (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 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

Propionic Acidemia (PA) (Organic Acidemia)

	Draniania Acidamia (DA)
Disease (common abbreviation) MIM #	Propionic Acidemia (PA) 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
This is a stage of the stage of	Plasma amino acids (PAA)
	Total homocysteine
	B12 levels in patient and mother
	Electrolytes (especially if sick)
Recommended additional testing to consider	Glucose
at time of initial consultation	Ammonia
	Carnitine, total and free
	Urine ketones
	Elevated 3-OH-propionate, propionylglycine, tiglylglycine,
	propionate(volatile, so not always detected) and
	methylcitrate (UOA)
	Elevated glycine (PAA)
Abor - was all Adatash alitas From a stand	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 ₁ Variant (Cbl
Differential Diagnosis	D ₁); Cobalamin C Cofactor Deficiency (Cbl C); Methylmalonic-
Dijjerentiai Diagnesis	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	www.acmg.net/StaticContent/ACT/C3.pdf
Sheet	www.acmg.net/staticcontent/Act/cs.put
American College of Medical Genetics	www.acma.not/StaticContent/ACT/Algorithms/Visio.C2.sdf
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3.pdf
Algorithm	
Algorithm Recommended Uniform Screening Panel	Core Panel

(RUSP)

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

(Organic Acidemia)	
Disease (common abbreviation) MIM # SNOMED Code / ICD-10-CM Code Enzyme or other abnormality MIM # / Enzyme Commission #	Beta-Oxothiolase Deficiency; Beta-Ketothiolase Deficiency (BKT) 203750 237953006 / E71.19 Beta-ketothiolase (mitochondrial acetoacetyl-CoA lyase) 607809 / 2.3.1.16
Abnormal Newborn Screening Metabolite(s) LOINC Number(s)	Elevated C5:1 53170-7 Elevated C5OH
Initial Diagnostics at Referral Center	Urine organic acids Plasma Acylcarnitine profile
Recommended additional testing to consider at time of initial consultation	Electrolytes Blood glucose
Abnormal Metabolites Expected	Elevated urinary tiglylglycine, 2-methyl-3OH-butyrate and 2-methylacetoacetate (UOA) Elevated tiglylcarnitine and 2-methyl-3-OH-butyrylcarnitine (Acylcarnitine) 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
Diagnostic Confirmation	Enzyme assay Mutation analysis: 0 mutation - disease unlikely (unless consanguineous) 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 (MHBD)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1536500%5BDISCUI% 5D&condition=C1536500&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)	Core Panel

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

	Jiganic Acidenna)
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
	Blood glucose
Recommended additional testing to consider	Urine glutaric and 3-OH-glutaric acid by stable isotope dilution
at time of initial consultation	Carnitine, total and free
	Elevated 3-OH-glutaric acid
	+/- glutaric acid (UOA)
	Elevated glutarylcarnitine (plasma and urine)
Abnormal Metabolites Expected	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)
been ruled out:	Persistently elevated 3-OH-glutaric acid
	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
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	DC (4 29 06).pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

	Jiganic Acidenna)
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
Initial Diagnostics at Referral Center	Urine organic acids (UOA)
milia. Diagnostics at hejerrar 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
	Electrolytes abnormalities are common in sick patients
	Blood glucose depends on fed status of patient
If initial testing is negative has the disorder	Yes
been ruled out?	103
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	
Sheet	www.acmg.net/StaticContent/ACT/C5-OH.pdf
American College of Medical Genetics	www.acmag.nat/CtatioComtont/ACT/Al-acitless-A/iaia-CT-OHII
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-OH.pdf
Recommended Uniform Screening Panel	Core Panel
(RUSP)	Core ranei

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

	Diganic Acidenna)
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	None
at time of initial consultation	Notic
	Elevated 3-hydroxyisovaleric acid and 3-methylcrotonylglycine
Abnormal Metabolites Expected	(UOA)
Abhormar Wetabolites Expected	Elevated C5OH
	*Maternal testing may indicate 3MCC
If initial testing is negative has the disorder	Yes (Consider maternal 3MCC)
been ruled out?	· · · · · · · · · · · · · · · · · · ·
	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-
Dijjerentiai Diagnosis	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.not/StatisContont/ACT/CE_OUL.ndf
Sheet	www.acmg.net/StaticContent/ACT/C5-OH.pdf
American College of Medical Genetics	www.acmg.not/StaticContont/ACT/Algorithms/A/isia CE OU adf
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-OH.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

	organie / telderina)
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
Initial Diagraphics at Referral 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 3-methylglutaconic acid, 3-methylglutaric acid and 3-
	hydroxyisovaleric acid (UOA)
Abnormal Metabolites Expected	Elevated C5OH
The normal wrecase mees expected	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)
Diamenting	NA. Astis a sussing is socially
Diagnostic Confirmation	Mutation analysis is available
	3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG); 3-
	Methylcrotonylglycinuria aka 3-Methylcrotonyl-CoA
Differential Diagnosis	Carboxylase Deficiency (3MCC); 3-Methylglutaconic Aciduria,
	Type I (3MGA II); 3-Methylglutaconic Aciduria, Type I (3MGA
	III); 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	www.acmg.not/StaticContont/ACT/CE_OH_ndf
Sheet	www.acmg.net/StaticContent/ACT/C5-OH.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-OH.pdf
Algorithm	www.acmg.net/olaticcontent/ACT/Algorithms/visio-co-OH.pdf
Recommended Uniform Screening Panel	Secondary Target
(RUSP)	Secondary ranget

Isovaleric Acidemia (IVA) (Organic Acidemia)

	Organic Acidemia)
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
Abnormal Metabolites Expected	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?	Tes
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	
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Malonic Aciduria (MA) (Organic Acidemia)

	Digatile 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
Initial Diversation at Defermal Contac	Urine organic acids (UOA)
Initial Diagnostics at Referral Center	Plasma Acylcarnitine profile
Recommended additional testing to consider	Lluin a katanaa
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	Yes
been ruled out?	res
	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	1/61 1/1 0 1 1 1/4 07/100 7 0 1/5
Sheet	www.acmg.net/StaticContent/ACT/C3-DC.pdf
American College of Medical Genetics	LIGHT OF THE STATE
Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3-DC.pdf
Recommended Uniform Screening Panel	Carandam, Tamak
(RUSP)	Secondary Target

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

,	2 Methylhytyryl Cheinyria (2MPC)
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
Abnormal Metabolites Expected	Electrolytes abnormalities are common in sick patients
The formal wick about CS 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	www.acmg.net/StaticContent/ACT/C5.pdf
Sheet	
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)

	Organic Acidemia)
Disease (common abbreviation)	2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase Deficiency
D 41D 4 11	(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
Lenve warmer (e)	Elevated C5OH
Initial Diagnostics at Referral Center	Urine organic acids
Tilliai Diagnostics at Nejerral 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	No
been ruled out?	140
	Mutation analysis:
	0 mutation - disease unlikely (unless consanguineous)
Diagnostic Confirmation	1 mutation - proceed to enzyme assay
Biagnostic confirmation	2 known or likely pathological mutations in trans confirms
	diagnosis
	Enzyme analysis
Differential Diagnosis	Beta-Oxothiolase Deficiency aka Beta-Ketothiolase Deficiency
Differential Diagnosis	(BKT)
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	www.acmg.net/StaticContent/ACT/C5-OH.pdf
Sheet	www.derng.net/staticcontent/Act/cs-on.put
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-OH.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

Biotinidase Deficiency (BIOT) (Other Genetic Condition)

D: / // //	D: 1: : 1 D (: : (DIOT)
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	Urine organic acids
at time of initial consultation	office organic acids
Ab	Decreased biotinidase activity
Abnormal Metabolites Expected	Urine organic acids are usually normal in the neonatal period
If initial testing is negative has the disorder	V
been ruled out?	Yes
Diagnostic Confirmation	Decreased or absent biotinidase activity in serum
Differential Diagnosis	Multiple Carboxylase Deficiency (MCD/ Holocarboxylase
Dijjerentiai 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.not/StaticContent/ACT/Dictinidaco.ndf
Sheet	www.acmg.net/StaticContent/ACT/Biotinidase.pdf
American College of Medical Genetics	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
Algorithm	Biotinidase.pdf
Recommended Uniform Screening Panel	Core Panel
(RUSP)	

Cystic Fibrosis (CF)

(Other Genetic Condition)

Disease (common abbreviation)	Cystic Fibrosis (CF)
MIM#	219700
SNOMED Code / ICD-10-CM Code	190905008 / E84
Enzyme or other abnormality	Cystic fibrosis transmembrane receptor (CFTR)
MIM # / Enzyme Commission #	602421 / None
	Elevated immunoreactive trypsinogen (IRT)
Abnormal Newborn Screening Metabolite(s)	48633-2
LOINC Number(s)	Presence or absence of CFTR mutations
	54083-1
Initial Diversation at Defermal Contact	Sweat test and confirmation of mutations detected on newborn
Initial Diagnostics at Referral Center	screening (if done)
Recommended additional testing to consider at time of initial consultation	Mutation analysis of the CFTR gene
Abnormal Matabolitas Exposted	Elevated sweat chloride >60 millieq/L
Abnormal Metabolites Expected	Pathologic CFTR mutations
If initial tacting is negative has the disorder	Yes for classical cases
If initial testing is negative has the disorder been ruled out?	Borderline sweat test range of 30-60 millieq/L may represent an
been ruled out!	intermediate phenotype and require further testing
Diagnostic Confirmation	Repeat sweat test and/or genetic analysis, especially if infant
Diagnostic Confirmation	shows clinical symptoms
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=1080[geneid]&co
Genetic Testing Registry	ndition=C0010674&compare labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1250/
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/CF.pdf
Sheet	
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-IRT.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Classical Galactosemia (GALT) (Other Genetic 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
Abnormal Newborn Screening Metabolite(s)	33288-2 (presence) 42906-8 (activity/volume)
LOINC Number(s)	Common mutation analysis (some states)
LOTIVE NUTIBET(S)	Elevated total galactose in some states
	54084-9
Initial Diagram action at Defermal Courter	RBC Galactose-1-phosphate (Gal-1-P)
Initial Diagnostics at Referral Center	RBC GALT activity
D	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 epimerase
been ruled out?	testing in states that report elevated galactose
been ruled out:	
Diagnostic Confirmation	Decreased GALT activity
	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
American College of Medical Genetics Algorithm	GALT:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-GALT.pdf
	Elevated Galactose + deficient GALT:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Hypergalactosemia.pdf
Recommended Uniform Screening Panel	
(RUSP)	Core Panel
[11031]	

Galactokinase Deficiency (GALK) (Other 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 54084-9
LOINC Number(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 initial consultation	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 epimerase
been ruled out?	testing in states that report elevated galactose
	RBC galactokinase activity
Diagnostic Confirmation	Mutation analysis in suspected cases
Differential Diagnosis	Galactosemia (GALT); Galactose Epimerase Deficiency (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
American College of Medical Genetics Algorithm	Elevated Galactose +/- deficient GALT:
	www.acmg.net/StaticContent/ACT/Algorithms/Visio-
	Hypergalactosemia.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

Galactose Epimerase Deficiency (GALE) (Other Genetic Condition)

Galactose Epimerase Deficiency (GALE)
230350
8849004 / E74.21
UDP-galactose-4-epimerase
606953 / 5.1.3.2
Elevated galactose in some states
54084-9
Galactose-1-phosphate (Gal-1-P)
Galactose-1-phosphate uridyltransferase (GALT) activity (testing
for epimerase deficiency done after testing for GALT)
Liver function tests
Urine reducing substances
Urine galactitol
Elevated Gal-1-P
Normal GALT
Normal liver function tests
Elevated urine reducing substances
Elevated urine galactitol
If GALT activity normal proceed to galactokinase and epimerase
testing in states that report elevated galactose
RBC epimerase activity
Galactosemia; Galactokinase Deficiency (GALK)
www.ncbi.nlm.nih.gov/gtr/tests/?term=C0751161%5BDISCUI%
5D&condition=C0751161&compare labs=1
www.ncbi.nlm.nih.gov/books/NBK51671/
Elevated Galactose +/- deficient GALT:
www.acmg.net/StaticContent/ACT/Galactose.pdf
Elevated Galactose +/- deficient GALT:
www.acmg.net/StaticContent/ACT/Algorithms/Visio-
<u>Hypergalactosemia.pdf</u>
Secondary Target

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

T all related towards and Deficiencies Course Couching
T-cell-related Lymphocyte Deficiencies: Severe Combined
Immunodeficiency (SCID)
Many
31323000/D81.1
T-Cell Receptor Excision Circles (TREC)
Flow cytometry measuring the absolute number of T-cells, B-
cells and NK cells
Repeat Newborn Screen (especially in premature infants),
Lymphocyte proliferation to mitogens, T-cell subsets (naïve,
memory and activated)
Low T cell number, variable B and NK cells numbers depending
on SCID etiology
Yes
i es
Varies by SCID subtype, needs referral to Specialty Center
Many SCID subtypes and other immunodeficiencies are
associated with T-cells lymphopenia. Chromosome 22q11
deletion syndrome (DiGeorge syndrome) is a common
differential diagnosis. Premature infants without a hereditary
immunodeficiency are also more likely to have low TREC
values.
http://www.ncbi.nlm.nih.gov/gtr/tests/?term=C0085110[DISCU
I]&condition=C0085110&compare labs=1
ijacondition-coooditoacompale labs-1
X-SCID http://www.ncbi.nlm.nih.gov/books/NBK1410/,
ADA Deficiency http://www.ncbi.nlm.nih.gov/books/NBK1483/ ,
www.acmg.net/StaticContent/ACT/SCID.pdf
www.acmg.net/staticcontent/ACT/SCID.pdf
l la development
In development
In development Core

Fabry Disease (Lysosomal Storage Disorder)

(2)303	offial 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
	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 Sheet	www.acmg.net/StaticContent/ACT/Fabry.pdf
American College of Medical Genetics Algorithm	In development
Recommended Uniform Screening Panel (RUSP)	Not on Panel

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

	indi storage bisoraci y
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
Initial Diagnostics at Referral Center	Repeat ASM activity
Initial Diagnostics at Nejerral 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?	res
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 development
Recommended Uniform Screening Panel	Not on Panel
(RUSP)	Troc on Fanci

Gaucher Disease; Glucocerebrosidase Deficiency; Glucosylceramidase Deficiency, not including Saposin C Deficiency

(Lysosomal Storage Disorder)

	<u>, </u>
	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
	If no family history, repeat enzyme activity and perform GBA
Initial Diagnostics at Potorral Contar	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	Notice
Abnormal Metabolites Expected	Deficient glucocerebrosidase activity
If initial testing is negative has the disorder	?Yes
been ruled out?	! les
Diagnostic Confirmation	Deficient glucocerebrosidase activity
Differential Diagnosis	None
Specific Testing Laboratories as listed in	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=Glucosylceramid
GeneTests	ase Deficiency&condition=C0017205&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1269/
American College of Medical Genetics ACT	
Sheet	www.acmg.net/StaticContent/ACT/Gaucher.pdf
American College of Medical Genetics	In development
Algorithm	in development
Recommended Uniform Screening Panel	Not on Panel
(RUSP)	THOUGHT ANCI

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

(0.70080	
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
Initial Diagnostics at Referral Center	Mutation analysis of <i>GAA</i>
Initial Diagnostics at Negerial Center	Determine cross-reactive immunologic material (CRIM) status
	Cardiac evaluation (echocardiogram (EKG))
Recommended additional testing to consider	Serum creatine kinase (CK)
at time of initial consultation	Urine glucose tetrasaccharide (Glc4)
at time of initial consultation	Alanine aminotransferase (ALT)
	Deficient GAA activity
Abnormal Metabolites Expected	Elevated CK
Abnormal Metabolites Expected	Elevated Glc4
	Elevated ALT
If initial testing is negative has the disorder	Yes
been ruled out?	l les
Diagnostic Confirmation	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	1/01 1/10 1 1/10 07/10
Sheet	www.acmg.net/StaticContent/ACT/Pompe.pdf
American College of Medical Genetics	In dayalanment
Algorithm	In development
Recommended Uniform Screening Panel	Core
(RUSP)	COLE

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

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

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

Hurler Syndrome; Mucopolysaccharidosis, Type I (MPS I)
607014
7561003 / E76.01
α-L-iduronidase (IDUA)
252800/3.2.1.76
Deficient IDUA
55909-6
Repeat IDUA
Urine glucosaminoglycans (GAG)
Mutatian analysis of IDIIA
Mutation analysis of IDUA
Increased heparin and dermatan sulfate (a GAG)
Vo.
Yes
Deficient IDUA
None
www.ncbi.nlm.nih.gov/gtr/tests/?term=C0023786%5BDISCUI%
5D&condition=C0023786&compare labs=1
www.ncbi.nlm.nih.gov/books/NBK1162/
No ACT sheet
IND ACT SHEET
No algorithm
NO digoritriiri
Not on panel
Not on panel

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 Divergentias at Defermal Contac	Repeat iduronate sulfatase activity
Initial Diagnostics at Referral Center	Urine GAG
Recommended additional testing to consider	Mutation analysis of IDS
at time of initial consultation	Widtation analysis of 103
Abnormal Matabolitas Expected	Deficient iduronate sulfatase activity
Abnormal Metabolites Expected	Increased dermatan and heparan sulfate (GAG)
If initial testing is negative has the disorder	Vec
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	No ACT sheet
Sheet	TWO NOT SHEEL
American College of Medical Genetics	No algorithm
Algorithm	
Recommended Uniform Screening Panel	Not on Panel
(RUSP)	Troc on Fanci

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

(L)353511141 Storage Disoraer)	
Disease (common abbreviation)	Maroteaux-Lamy Syndrome; Mucopolysaccharidosis Type VI
MIM #	(MPS VI)
SNOMED Code / ICD-10-CM Code	253200
Enzyme or other abnormality	69463008 / E76.29
MIM # / Enzyme Commission #	Arylsulfatase B (ARSB)
· ,	611542 / 3.1.6.12
Abnormal Newborn Screening Metabolite(s)	Deficient ARSB activity
LOINC Number(s)	2646-8 (Enzymatic activity, serum)
Initial Diagnostics at Referral Center	Repeat arylsulfatase B activity
mittal Diagnostics at Nejerral center	Urine GAG
Recommended additional testing to consider at time of initial consultation	Mutation analysis of ARSB
Abor a mar al Adata balita a Front attack	Deficient ARSB activity
Abnormal Metabolites Expected	Increased dermatan sulfate (GAG)
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Deficient ARSB activity
Differential Diagnosis	None
Specific Testing Laboratories as listed in the	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0026709%5BDISCUI%
Genetic Testing Registry	5D&condition=C0026709&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)	Not on Panel

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

D: / // // //	, , , , , , , , , , , , , , , , , , ,
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
heiting Diagramenting at Defermed Courter	Very Long-Chain Fatty Acid (Peroxisomal) Analysis
Initial Diagnostics at Referral Center	Confirmatory mutation analysis
Recommended additional testing to consider	Plasmalogen analysis in patients with no identified mutation on
at time of initial consultation	newborn screening
	Elevated C26:0, Elevated ratios C24:0/C22:0, C26:0/C22:0
Abnormal Metabolites Expected	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
Diagnostic Confirmation	
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	n=C0162309&compare labs=1
	<u> </u>
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1315/
American College of Medical Genetics ACT	No ACT sheet
Sheet	NO ACT SHEEL
American College of Medical Genetics	No algorithm
Algorithm	I NO BIROLIUIII
Recommended Uniform Screening Panel	No.
(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 B₁₂ Vitamin B₁₂, cobalamin

BAER Brainstem auditory evoked response

BCKD Branched-chain alpha-keto acid dehydrogenase

BIOT Biotinidase deficiency, Biotinidase BKT 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 D₁ Cobalamin D₂ cofactor
Cbl D₂ Cobalamin D₂ 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

HbSB⁰ Sickle cell beta zero thalassemia HbSB⁺ 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, 10th 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
Phenylalanina

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

SUCLA₁ Succinate-CoA lyase, alpha subunit SUCLA₂ 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