NYMAC

New York – Mid-Atlantic Consortium for Genetic and Newborn Screening Services

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Diagnostic Guidelines for Confirmation of Screen-Positive Newborn Screening Results

Updated:
September 2014

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Congenital Adrenal Hyperplasia (CAH)
(Endocrine Disorder)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Congenital Adrenal Hyperplasia (CAH) (non-classical; salt-wasting; simple virilizing) 201910 237754008; 71578002; 52604008 / E25.0 21-Hydroxylase 201910 / 1.14.99.10
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated 17-hydroxyprogesterone (17-OHP) 38473-5
Initial Diagnostics at Referral Center	Serum 17-OHP Serum electrolytes Blood glucose
Recommended additional testing to consider at time of initial consultation	Clinical suspicion low: None Clinical suspicion high: Steroid profile ACTH stimulation test Mutation analysis
Abnormal Metabolites Expected	Severe: Markedly elevated 17-OHP 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)*
Diagnostic Confirmation	Markedly elevated 17-OHP is diagnostic of severe CAH Mild to moderate 17-OHP elevation do: Steroid profile ACTH stimulation test Mutation analysis
Differential Diagnosis	Stress, prematurity
Specific Testing Laboratories as listed in Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0852654%5BDISCUI%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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-NBS_Elevated_17OHP.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: www.acmg.net/StaticContent/ACT/Primary_TSH.pdf Low T4/Elevated TSH: www.acmg.net/StaticContent/ACT/Primary_T4_Followup.pdf
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/Beta^0 Thalassemia (HbSB^0), and Sickle C Disease (HbSC) (Hemoglobinopathy)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Sickle Cell Disease including Hemoglobin SS (SS), Hemoglobin S/Beta$^+$ Thalassemia (HbSß$^+$), Hemoglobin S/Beta^0 Thalassemia (HbSß^0) and Sickle C Disease (HbSC) 603903 (SS); 141900 (Others) Multiple / Multiple Beta globin MIM # 141900 / N/A
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	FS, FSA, FSC, etc. 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	FS, FSA, FSC, etc. CBC abnormalities may be expected depending on the disorder; newborn CBC normal in SS
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	SS: www.ncbi.nlm.nih.gov/gtr/tests/?term=C0002895%5BDISCUI%5D&condition=C0002895&compare_labs=1 HbSß^O, HbSß$^+$: www.ncbi.nlm.nih.gov/gtr/tests/?term=C0221019%5BDISCUI%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/
American College of Medical Genetics ACT Sheet	HbSS, HbSß^0: www.acmg.net/StaticContent/ACT/ACT_sheet_HBSS_FS__4.28.06%20ljo.pdf 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
American College of Medical Genetics Algorithm	All Hemoglobinopathies: 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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Other Hemoglobinopathies 141900 Multiple / Multiple Beta globin 141900 / N/A
Abnormal Newborn Screening Metabolite(s) *LOINC Number*	FVar, etc. 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-Hemoglobinopathy_4.18.06.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Sickle Cell Carrier (HbAS)
(Hemoglobinopathy)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Sickle Cell Carrier (HbAS) 141900 Multiple / Multiple Beta globin 141900 / N/A
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	FAS 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 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 Sheet	www.acmg.net/StaticContent/ACT/ACT_sheet_Hb_carrier_trait_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)

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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Argininosuccinic Lyase Deficiency; Argininosuccinic Aciduria (ASA) 207900 41013004 / E72.22 Argininosuccinic lyase 608310 / 4.3.2.1
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated citrulline (some states elevated ASA) 42892-0
Initial Diagnostics at Referral Center	Plasma amino acids (PAA) Urine orotic acid
Recommended additional testing to consider at time of initial consultation	Liver function tests Ammonia
Abnormal Metabolites Expected	Elevated citrulline, glutamine, and argininosuccinic acid (PAA) Decreased arginine (PAA) Elevated urine orotic acid possible Normal liver function tests expected Elevated ammonia expected
If initial testing is negative has the disorder been ruled out?	Yes
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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268547%5BDISCUI%5D&condition=C0268547&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK51784/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/Citrullinemia.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-Citrulline.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

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

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

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

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

Homocystinuria (HCY)
(Amino Acidemia)

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

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

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

Maple Syrup Urine Disease (MSUD)
(Amino Acidemia)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Maple Syrup Urine Disease (MSUD) 248600 27718001 / E71.0 Branched-chain alpha-keto acid dehydrogenase (BCKD) 608348 / 1.2.4.4
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated leucine + isoleucine 53152-5
Initial Diagnostics at Referral Center	Plasma amino acids (PAA) Urine organic acids (UOA)
Recommended additional testing to consider at time of initial consultation	Urine ketones
Abnormal Metabolites Expected	Elevated leucine, isoleucine, valine and alloisoleucine (PAA) Abnormal branched-chain ketoacids (UOA) Elevated urinary ketones
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Elevated branched-chain amino acids and elevated alloisoleucine 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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0024776%5BDISCUI%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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-Leucine.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Phenylketonuria (PKU) and Hyperphenylalaninemia (H-PHE) 261600 7573000 / E70.0 Phenylalanine hydroxylase 261600 / 1.14.16.1
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated phenylalanine 29573-3
Initial Diagnostics at Referral Center	Plasma amino acids (PAA)
Recommended additional testing to consider at time of initial consultation	Urine biopterin and neopterin Dihydropteridine reductase activity
Abnormal Metabolites Expected	Elevated phenylalanine levels 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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0031485%5BDISCUI%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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-Phenylalanine.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Tyrosinemia Type I (TYR-I) 276700 410056006 / E70.21 Fumarylacetoacetase hydrolase (FAH) 276700 / 3.7.1.2
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated tyrosine(tyrosine may be normal at the time of the first screen) 35571-9 Elevated succinylacetone 53231-7
Initial Diagnostics at Referral Center	Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests
Recommended additional testing to consider at time of initial consultation	Alpha fetoprotein
Abnormal Metabolites Expected	Elevated tyrosine, methionine (PAA) Elevated succinylacetone and succinylacetoacetate (UOA) 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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268490%5BDISCUI%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)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Tyrosinemia Type II (TYR-II) 276600 4887000 / E70.21 Tyrosine aminotransferase 613018 / 2.6.1.5
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated tyrosine 35571-9 Normal succinylacetone 53231-7
Initial Diagnostics at Referral Center	Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests
Recommended additional testing to consider at time of initial consultation	Alpha fetoprotein
Abnormal Metabolites Expected	Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes
Differential Diagnosis	Tyrosinemia Type I (TYR I); Tyrosinemia Type III (TYR III); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268487%5BDISCUI%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
American College of Medical Genetics Algorithm	Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated,_SUAC_normal.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Tyrosinemia Type III (TYR-III); 4-Hydroxyphenylpyruvic Acid Oxidase Deficiency 276710 415764005 / E70.21 4-Hydroxyphenylpyruvic acid oxidase 276710 / 1.13.11.27
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated tyrosine 35571-9 Normal succinylacetone 53231-7
Initial Diagnostics at Referral Center	Plasma amino acids (PAA) Urine organic acids (UOA) including succinylacetone Liver function tests
Recommended additional testing to consider at time of initial consultation	Alpha fetoprotein
Abnormal Metabolites Expected	Elevated tyrosine (PAA) Elevated 4-OH-phenylpyruvate, 4-OH-phenyllactate, 4-tyramine, N-acetyltyrosine (UOA) Normal succinylacetone (UOA) Normal liver function tests expected Normal alpha fetoprotein (after neonatal period)
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Persistence of tyrosine elevation, with negative succinylacetone Needs to be differentiated from transient tyrosinemia of the newborn (TTN) and nongenetic causes
Differential Diagnosis	Tyrosinemia Type I (TYR I); Tyrosinemia Type II (TYR II); Total Parenteral Nutrition (TPN), Transient Tyrosinemia of the Newborn
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268623%5BDISCUI%5D&condition=C0268623&compare_labs=1
Specific Testing Laboratories as listed in the Genetic Testing Registry	
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/Tyrosine.pdf
American College of Medical Genetics Algorithm	Tyrosine elevated; succinylacetone normal: www.acmg.net/StaticContent/ACT/Algorithms/Visio-Tyrosine_elevated,_SUAC_normal.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Carnitine Palmitoyl Transferase Type Ia Deficiency (CPT-Ia) 255120 238001003 / E71.314 Carnitine palmitoyl transferase Ia 600528 / 2.3.1.21
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C0 38481-8 Elevated C0/(C16+C18) ratio* 53235-8
Initial Diagnostics at Referral Center	Carnitine, total and free in blood spot (<1 wk) Carnitine, total and free in plasma (>1 wk) Plasma acylcarnitine profile Blood spot Acylcarnitine profile
Recommended additional testing to consider at time of initial consultation	Liver function tests Blood glucose
Abnormal Metabolites Expected	Normal/elevated carnitine Decreased C16 and C18 Elevated C0/(C16+C18) (blood spot < 1 wk) 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 been ruled out?	Yes
Diagnostic Confirmation	* If initial C0/(C16+C18) ratio >100 or if expected abnormal metabolites are seen (Blood spot ratios valid in infants less 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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342789%5BDISCUI%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 Sheet	www.acmg.net/StaticContent/ACT/C0_C16-C18.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C0.vsd;_C0.vsd;C16-C18.pdf
Recommended Uniform Screening Panel (RUSP)	Secondary Target

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 #*	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
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	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 #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Carnitine-Acylcarnitine Translocase Deficiency (CACT) 255110 238003000 / E71.318 Carnitine-acylcarnitine translocase 212138 / 2.3.1.21
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C16 53199-6 Elevated C18:1 53202-8
Initial Diagnostics at Referral Center	Carnitine, total and free in plasma Acylcarnitine profile in plasma
Recommended additional testing to consider at time of initial consultation	Creatinine phosphokinase (CPK) Blood glucose
Abnormal Metabolites Expected	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	Mutation analysis with detection of two known or likely pathological mutations in trans
Differential Diagnosis	Carnitine Palmitoyl Transferase Type II Deficiency (CPT II)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342791%5BDISCUI%5D&condition=C0342791&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/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 Uptake Defect (CUD); Primary Carnitine Deficiency (Fatty Acid Oxidation Disorder)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Carnitine Uptake Defect (CUD); Primary Carnitine Deficiency 212140 21764004 / E71.41 Plasma membrane carnitine transporter 603377 / None
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Decreased C0 38481-8 Decreased SUM (Acylcarnitines) None
Initial Diagnostics at Referral Center	Plasma Carnitine, total and free Acylcarnitine profile Urine Carnitine, total and free
Recommended additional testing to consider at time of initial consultation	Creatinine phosphokinase (CPK) Blood glucose
Abnormal Metabolites Expected	Decreased carnitine, total and free Decreased acylcarnitines (long-chain) Elevated total and free urine carnitine Reduced carnitine renal reabsorptiom CPK can be elevated in sick patients Blood glucose depends on fed status of patient
If initial testing is negative has the disorder been ruled out?	Yes (provided no carnitine supplementation)
Diagnostic Confirmation	Enzyme assay (OCTN2) in fibroblasts and/or mutation analysis if functional assay unclear Consider maternal testing
Differential Diagnosis	Consider other non-genetic causes of carnitine deficiency – nutritional, renal insufficiency, other primary IEMs and maternal CUD or IEMs
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342788%5BDISCUI%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 Sheet	www.acmg.net/StaticContent/ACT/C0.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C0.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD) 609016 237999008 / E71.310 Long-chain L3-Hydroxyacyl-CoA dehydrogenase 600890 / 1.1.1.211
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C16OH 50125-4 Elevated C18:1OH 50113-0
Initial Diagnostics at Referral Center	Acylcarnitine profile Urine organic acids Mutation analysis, as negative metabolites do not rule out the disorder
Recommended additional testing to consider at time of initial consultation	Liver function tests Blood glucose Creatinine phosphokinase (CPK) Plasma Carnitine, total and free
Abnormal Metabolites Expected	Elevated C16OH, C18:1OH (acylcarnitines) Elevated 3-OH-dicarboxylic acids (C6-C14), saturated and unsaturated, (UOA) which are only be seen during episodes of metabolic decompensation, with normal or absent ketones Detection of known pathological 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 been ruled out?	Yes
Diagnostic Confirmation	Mutation analysis for combined LCHAD/TFP: 0 mutation - ruled out (unless consanguineous and as long as metabolites normal) 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 Genetic Testing Registry	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=C0342786[DISCUI]&condition=CN074230&compare_labs=1
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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD) 201450 128596003 / E71.311 Medium-chain acyl-CoA dehydrogenase 607008 / 1.3.99.3
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C8 53175-6 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 Urine organic acids and/or urine acylglycines
Recommended additional testing to consider at time of initial consultation	Blood glucose Plasma Carnitine, total and free
Abnormal Metabolites Expected	Elevated C6, C8, C10 (acylcarnitines) C6<C8>C10 Elevated hexanoylglycine and suberylglycine (acylglycines) Blood glucose depends on fed status of patient Normal/Low plasma carnitine levels Elevated dicarboxylic acids, especially suberic acid, with no excess ketones (UOA)
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Typical pattern of acylcarnitines is diagnostic - C6<C8>C10 Elevated urine hexanoglycine and suberylglycine Mutation analysis widely available
Differential Diagnosis	Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT); Multiple Acyl-CoA Dehydrogenase Deficiency (MADD)/(Glutaric Acidemia Type 2) (GA 2)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0220710%5BDISCUI%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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C8.vsd;_C6-C10.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT) 602199 124265004 / None Medium-chain ketoacyl-CoA thiolase None; sequence unknown / 2.3.1.16
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C6 and C8 45211-0, 53175-6
Initial Diagnostics at Referral Center	Acylcarnitine profile Urine organic acids
Recommended additional testing to consider at time of initial consultation	Blood glucose Urine ketones Plasma Carnitine, total and free Urine acylglycines Creatinine phosphokinase (CPK)
Abnormal Metabolites Expected	Elevated C6 and C8 Elevated ketones bodies on urine organic analysis Blood glucose depends on fed state of patient 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
Differential Diagnosis	Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD); Multiple Acyl-CoA Dehydrogenase Deficiency (MADD) (Glutaric Acidemia Type 2) (GA 2)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1865781%5BDISCUI%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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Multiple Acyl-CoA Dehydrogenase Deficiency (MADD); Glutaric Acidemia Type II (GA-II) 231680 22886006 / E71.313 Electron Transfer Flavoprotein (alpha, beta subunit) 608053, 130410, 231675 / 1.5.5.1
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C4, C5, C6, C8, C10 53166-5, 45216-9, 45211-0, 53175-6, 45197-1
Initial Diagnostics at Referral Center	Acylcarnitine profile Urine organic acids Urine acylglycines
Recommended additional testing to consider at time of initial consultation	Blood glucose Creatinine phosphokinase (CPK) Liver function tests
Abnormal Metabolites Expected	Elevated C4, C5, C6, C8, C10 and long-chain acylcarnitines Elevated lactate, 2-OH-glutarate, ethylmalonic acid and adipic acids (UOA) Elevated isovaleryl-, hexanoyl-, suberylglycine (acylglycines) Blood glucose depends on fed status of patient CPK may be elevated in sick patients Liver function tests may be abnormal in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Abnormal metabolite pattern is diagnostic If not found, need 1) Mutation analysis with two known or likely pathological mutations in trans, or 2) Enzyme/functional assay 'Grey Zone' can remain, could still be affected, but consider maternal disorder, mitochondrial disorder, riboflavin deficiency
Differential Diagnosis	Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD); Medium-chain Ketoacyl-CoA Thiolase Deficiency (MCKAT), Mitochondrial Disorder, Riboflavin Deficiency, Maternal Disorder
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268596%5BDISCUI%5D&condition=C0268596&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT 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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD) 201470 124166007 / E71.312 Short-chain acyl-CoA dehydrogenase 606885 / 1.3.99.2
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C4 53166-5
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma acylcarnitine profile Urine acylglycine levels Urine C4 acylcarnitines
Recommended additional testing to consider at time of initial consultation	Blood glucose Plasma Carnitine, total and free
Abnormal Metabolites Expected	Elevated ethylmalonic acid (UOA) Elevated butyrylglycine (urine acylglycines) +/- Elevated urine C4 levels Blood glucose depends on fed status of patient Normal/low carnitine levels
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Mutation analysis with 2 known or likely pathological mutations in trans
Differential Diagnosis	Ethylmalonic Encephalopathy (EMA); Isobutyryl-CoA Dehydrogenase Deficiency (IBCD); presence of SCAD polymorphisms
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=short-chain+acyl+coa
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK63582/
American College of Medical Genetics ACT 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)	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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Medium/Short-chain L-3-Hydroxyacyl-CoA Dehydrogenase Deficiency (M/SCHAD); 3-@Hydroxyacyl-Co-A Dehydrogenase Deficiency (HADH) 231530 237998000 / None Short-chain L-3-hydroxyacyl-CoA dehydrogenase 601609 / 1.1.1.35
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C4OH 50102-3
Initial Diagnostics at Referral Center	Plasma acylcarnitine profile Urine organic acids Plasma 3-OH-fatty acids Glucose Insulin
Recommended additional testing to consider at time of initial consultation	Free fatty acids
Abnormal Metabolites Expected	Elevated C4OH Elevated/normal ketone bodies on urine organic analysis 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
Diagnostic Confirmation	Enzyme analysis in blood leukocytes Mutation analysis
Differential Diagnosis	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=Hydroxyacyl-CoA Dehydrogenase Deficiency &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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Trifunctional Protein Deficiency (TFP) 609015 237999008 / E88.39 Trifunctional protein (alpha, beta subunit) 600890, 143450 / 1.1.1.211
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C16OH 50125-4 Elevated C18:1OH 50113-0
Initial Diagnostics at Referral Center	Acylcarnitine profile Urine organic acids Mutation analysis, as negative metabolites do not rule out the disorder
Recommended additional testing to consider at time of initial consultation	Liver function tests Blood glucose Creatinine phosphokinase (CPK) Plasma Carnitine, total and free
Abnormal Metabolites Expected	Elevated C16OH, C18:1OH (acylcarnitines) Elevated 3-OH-dicarboxylic acids (C6-C14) , saturated and unsaturated (UOA) which are only be seen during episodes of metabolic decompensation, with normal or absent ketones Detection of known pathological mutations in trans Liver function tests may be abnormal in sick patients Blood glucose depends on fed status of patient CPK may be elevated in sick patients Normal/low carnitine levels
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Mutation analysis for combined LCHAD/TFP: 0 mutation – disease unlikely (unless consanguineous and as long as metabolites normal) 1 known or likely pathological mutation - proceed to enzyme assay or functional (probe) study 2 known or likely pathological mutations in trans – diagnosis confirmed
Differential Diagnosis	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=C0342786%5BDISCUI%5D&condition=C0342786&compare_labs=1
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

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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Ethylmalonic Encephalopathy (EMA) 602473 81308009 / G93.41 ETHE1 protein 608451 / 1.5.5.1
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C4 and C5 53166-5/??? Elevated C4/C3 ratio 53168-1 Elevated C5/C2 ratio 53239-0
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Acylcarnitine profile Urine acylglycine levels (UAG) (urine C4 acylcarnitines)
Recommended additional testing to consider at time of initial consultation	Blood glucose Carnitine, total and free
Abnormal Metabolites Expected	Elevated ethylmalonic acid, methylsuccinic acid and lactate (UOA) Elevated C4 in plasma and urine Elevated isobutyrylglycine and 2-methylbutyrylglycine (UAG) Blood glucose depends on fed status of patient Normal/low plasma carnitine levels
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Abnormal metabolite pattern with clinical phenotype Mutation analysis with two known or likely pathological mutations in trans (may not be available in US)
Differential Diagnosis	Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD); Isobutyryl-CoA Dehydrogenase Deficiency (IBCD)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1865349%5BDISCUI%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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Isobutyryl-CoA Dehydrogenase Deficiency (IBCD); Isobutyrylgylcinuria (IBG) 604773 124136000 / E71.19 Isobutyryl-CoA dehydrogenase 604773 / 1.1.1.157
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C4 53166-5
Initial Diagnostics at Referral Center	Urine organic acids Acylcarnitine profile Urine acylglycine levels Urine C4 acylcarnitines
Recommended additional testing to consider at time of initial consultation	Blood glucose Carnitine, total and free
Abnormal Metabolites Expected	Elevated C4 in plasma and urine Normal ethylmalonic acid Elevated isobutyrylglycine Blood glucose depends on feeding 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, and mutation analysis with two known or likely pathological mutations in trans
Differential Diagnosis	Ethylmalonic Encephalopathy (EMA); Short-chain Acyl-CoA Dehydrogenase Deficiency (SCAD)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1969809%5BDISCUI%5D&condition=C1969809&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)	Secondary Target

Methylmalonic Acidemia - Cobalamin A,B Cofactor Deficiency (Cbl A,B); Cobalamin D_1 Cofactor Deficiency ($CblD_1$)
(Organic Acidemia)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM #* */ Enzyme Commission #*	Methylmalonic Aciduria - Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D_1 Cofactor Deficiency (Cbl D_1) 251100 (A), 251110 (B) 73843004 (A), 82245003 (B) / E71.120 Cobalamin A,B cofactor deficiency 607481 (A), 607568 (B) Cobalamin D_1 cofactor 611935 / 5.4.99.2
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C3 53160-8 Elevated C4DC 45222-7
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma Acylcarnitine profile Plasma methylmalonic acid (MMA) Plasma amino acids Total homocysteine B_{12} levels in patient and mother
Recommended additional testing to consider at time of initial consultation	Electrolytes (especially if sick) Blood glucose Ammonia Carnitine, total and free Urine ketones
Abnormal Metabolites Expected	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) Normal total homocysteine and B_{12} levels Electrolytes abnormalities are common in sick patients Blood glucose depends on fed status of patient Ammonia can be elevated in sick patients Normal/low carnitine levels Elevated urine ketones, especially in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Elevated methylmalonic acid in blood and urine Mutation analysis: 0 mutation - disease ruled out (unless consanguineous) 1 mutation - proceed to enzyme assay 2 mutations in trans – diagnosis confirmed Complementation studies in fibroblasts
Differential Diagnosis	Cobalamin C Cofactor Deficiency (Cbl C); Cobalamin D_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 D_2 Cofactor Deficiency (Cbl D_2), Cobalamin F Cofactor Deficiency (Cbl F); Cobalamin J Cofactor Deficiency (Cbl J)
(Organic Acidemia)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM #* */ Enzyme Commission #*	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) 609831 MMADHC protein (Cobalamin D_2 cofactor) 611935 / 5.4.99.2; None LMBRD1 (Cobalamin F cofactor) 612625 / Cobalamin J cofactor not found in OMIM
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C3 53160-8 Elevated C4DC 45222-7 (?low methionine in some states)
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma acylcarnitine profile Plasma methylmalonic acid (MMA) Plasma amino acids (PAA) Total homocysteine B12 levels in patient and mother
Recommended additional testing to consider at time of initial consultation	Electrolytes (especially if sick) Blood glucose Ammonia Carnitine, total and free Urine ketones
Abnormal Metabolites Expected	Elevated total homocysteine Elevated MMA (UOA) Normal amino acids (may have elevated free homocystine and low methionine) (PAA) 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 been ruled out?	Yes
Diagnostic Confirmation	Elevated total plasma homocysteine and elevated methylmalonic acid in blood and urine Mutation analysis: 0 mutation - disease ruled out (unless consanguineous) 1 mutation - proceed to enzyme assay 2 mutations in trans confirms diagnosis.

	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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Multiple Carboxylase Deficiency (MCD) 253270 15307001 / D81.81 Holocarboxylase synthetase (HCS) 609018 / 6.3.4.11
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C3 53160-8 Elevated C5OH 45207-8
Initial Diagnostics at Referral Center	Urine organic acid (UOA) Plasma Acylcarnitine profile Biotinidase assay if not done by state newborn screening program Lactate
Recommended additional testing to consider at time of initial consultation	Electrolytes Glucose Ammonia
Abnormal Metabolites Expected	Elevated 3-OH-isovaleric acid, lactate, tiglylglycine, 3-methylcrotonylglycine, methylcitrate, 3-OH propionate (UOA) Elevated C5OH and C3 (plasma acylcarnitines) 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
Diagnostic Confirmation	Mutation analysis: 0 mutation - disease unlikely (unless consanguineous) 1 mutation - proceed to enzyme assay 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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268581%5BDISCUI%5D&condition=C0268581&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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Methylmalonyl-CoA Mutase Deficiency (MUT) 251000 124680001 / E71.120 Methylmalonyl-CoA mutase 251000 / 5.4.99.2
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C3 53160-8 Elevated C4DC 45222-7
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma Acylcarnitine profile Plasma methylmalonic acid Plasma amino acids (PAA) Total homocysteine B_{12} levels in patient and mother
Recommended additional testing to consider at time of initial consultation	Electrolytes (especially if sick) Blood glucose Ammonia Carnitine, total and free Urine ketones
Abnormal Metabolites Expected	Elevated methylmalonic acid (UOA and in plasma) Elevated 3-OH-propionic acid, methylcitric acid, (UOA) Elevated glycine (PAA) Normal homocysteine and B_{12} levels Electrolytes abnormalities are common in sick patients Blood glucose depends on fed status of patient Ammonia can be elevated in sick patients Normal/low carnitine levels Elevated urine ketones especially in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Mutation analysis: 0 mutation disease unlikely (unless consanguineous) 1 mutation - proceed to enzyme assay 2 known or likely pathological mutations in trans confirms diagnosis Complementation studies in fibroblasts
Differential Diagnosis	Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D_1 Variant (Cbl D_1); Cobalamin C Cofactor Deficiency (Cbl C) (normal or increased homocysteine); Cobalamin D_2 Cofactor Deficiency (Cbl D_2) (increased homocysteine); Propionic Acidemia (PA)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C1855114%5BDISCUI%5D&condition=C1855114&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT	www.acmg.net/StaticContent/ACT/C3.pdf

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

Propionic Acidemia (PA)
(Organic Acidemia)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Propionic Acidemia (PA) 606054 69080001 / E71.121 Propionyl-CoA carboxylase 232000, 232050 / 6.4.1.3
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C3 53160-8
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma Acylcarnitine profile Plasma methylmalonic acid Plasma amino acids (PAA) Total homocysteine B12 levels in patient and mother
Recommended additional testing to consider at time of initial consultation	Electrolytes (especially if sick) Glucose Ammonia Carnitine, total and free Urine ketones
Abnormal Metabolites Expected	Elevated 3-OH-propionate, propionylglycine, tiglylglycine, propionate(volatile, so not always detected) and methylcitrate (UOA) Elevated glycine (PAA) Normal methylmalonic acid and homocysteine Electrolytes abnormalities are common in sick patients Blood glucose depends on fed status of patient Ammonia can be elevated in sick patients Normal/low carnitine levels Elevated urine ketones especially in sick patients
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Elevated propionate and methylcitrate generally accepted for diagnosis
Differential Diagnosis	Cobalamin A,B Cofactor (Cbl A,B); Cobalamin D_1 Variant (Cbl D_1); Cobalamin C Cofactor Deficiency (Cbl C); Methylmalonic-CoA Mutase Deficiency (MUT)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268579%5BDISCUI%5D&condition=C0268579&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK92946/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C3.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C3.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Glutaric Acidemia Type I (GA-I) 231670 76175005 / E72.3 Glutaryl-CoA dehydrogenase 608801 / 1.3.99.7
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C5DC 45207-8
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma Acylcarnitine profile Urine glutarylcarnitine
Recommended additional testing to consider at time of initial consultation	Blood glucose Urine glutaric and 3-OH-glutaric acid by stable isotope dilution Carnitine, total and free
Abnormal Metabolites Expected	Elevated 3-OH-glutaric acid +/- glutaric acid (UOA) Elevated glutarylcarnitine (plasma and urine) 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)
Diagnostic Confirmation	Persistently elevated 3-OH-glutaric acid 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	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268595%5BDISCUI%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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/C5-DC_(4_29_06).pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG) 246450 124611007 / E71.19 3-Hydroxy-3-Methylglutaryl-CoA Lyase 246450 / 4.1.3.4
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C5OH 50106-4 Elevated C6DC 53187-1
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma acylcarnitine profile
Recommended additional testing to consider at time of initial consultation	Electrolytes Blood glucose
Abnormal Metabolites Expected	Elevated 3-hydroxyisovaleric acid, 3-methylglutaconic acid, 3-methylglutaric acid, 3-hydroxy-3-methylglutarate (UOA) 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 been ruled out?	Yes
Diagnostic Confirmation	Abnormal metabolite pattern confirms diagnosis
Differential Diagnosis	3-Methylcrotonylglycinuria aka 3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC); 3-Methylglutaconic Aciduria (3MGA)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268601%5BDISCUI%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 Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5-OH.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

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

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

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

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

Isovaleric Acidemia (IVA)
(Organic Acidemia)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Isovaleric Acidemia (IVA) 243500 87827003 / E71.110 Isovaleryl-CoA dehydrogenase 607036 / 1.3.99.10
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated C5 45216-9
Initial Diagnostics at Referral Center	Urine organic acids (UOA) Plasma Acylcarnitine profile Urine acylglycines
Recommended additional testing to consider at time of initial consultation	Electrolytes Urine ketones Blood glucose Ammonia
Abnormal Metabolites Expected	Elevated isovalerylglycine, isovaleric acid and 3-OH-isovaleric acid (UOA) Elevated isovalerylcarnitine (C5) Elevated isovalerylglycine 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 been ruled out?	Yes
Diagnostic Confirmation	Elevated isovalerylglycine, absent 2-methylbutyrlglycine
Differential Diagnosis	2-Methylbutyryl Glycinuria (2MBG)
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268575%5BDISCUI%5D&condition=C0268575&compare_labs=1
GeneReviews	None
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/C5.pdf
American College of Medical Genetics Algorithm	www.acmg.net/StaticContent/ACT/Algorithms/Visio-C5.pdf
Recommended Uniform Screening Panel (RUSP)	Core Panel

Malonic Aciduria (MA)
(Organic Acidemia)

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

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

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

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

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

Biotinidase Deficiency (BIOT)
(Other Genetic Condition)

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

Cystic Fibrosis (CF)
(Other Genetic Condition)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Cystic Fibrosis (CF) 219700 190905008 / E84 Cystic fibrosis transmembrane receptor (CFTR) 602421 / None
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Elevated immunoreactive trypsinogen (IRT) 48633-2 Presence or absence of CFTR mutations 54083-1
Initial Diagnostics at Referral Center	Sweat test and confirmation of mutations detected on newborn screening (if done)
Recommended additional testing to consider at time of initial consultation	Mutation analysis of the CFTR gene
Abnormal Metabolites Expected	Elevated sweat chloride >60 millieq/L Pathologic CFTR mutations
If initial testing is negative has the disorder been ruled out?	Yes for classical cases Borderline sweat test range of 30-60 millieq/L may represent an intermediate phenotype and require further testing
Diagnostic Confirmation	Repeat sweat test and/or genetic analysis, especially if infant shows clinical symptoms
Differential Diagnosis	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=1080[geneid]&condition=C0010674&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1250/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/CF.pdf
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) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Classical Galactosemia (GALT) 230400 398664009 / E74.21 Galactose-1-Phosphate Uridyltransferase 606999 / 2.7.7.12
Abnormal Newborn Screening Metabolite(s) LOINC Number(s)	Decreased GALT activity 33288-2 (presence) 42906-8 (activity/volume) Common mutation analysis (some states) Elevated total galactose in some states 54084-9
Initial Diagnostics at Referral Center	RBC Galactose-1-phosphate (Gal-1-P) RBC GALT activity
Recommended additional testing to consider at time of initial consultation	Liver function tests Urine reducing substances Urine galactitol
Abnormal Metabolites Expected	Elevated Gal-1-P Decreased GALT activity Liver function tests may be abnormal in sick patients Elevated urine reducing substances Elevated urine galactitol
If initial testing is negative has the disorder been ruled out?	If GALT activity normal proceed to galactokinase and epimerase testing in states that report elevated galactose
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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0268151%5BDISCUI%5D&condition=C0268151&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1518/
American College of Medical Genetics ACT Sheet	GALT: www.acmg.net/StaticContent/ACT/GalactosePlusGALT.pdf 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

Galactokinase Deficiency (GALK)
(Other Genetic Condition)

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

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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	T-cell-related Lymphocyte Deficiencies: Severe Combined Immunodeficiency (SCID) Many 31323000/D81.1
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	T-Cell Receptor Excision Circles (TREC)
Initial Diagnostics at Referral Center	Flow cytometry measuring the absolute number of T-cells, B-cells and NK cells
Recommended additional testing to consider at time of initial consultation	Repeat Newborn Screen (especially in premature infants), Lymphocyte proliferation to mitogens, T-cell subsets (naïve, memory and activated)
Abnormal Metabolites Expected	Low T cell number, variable B and NK cells numbers depending on SCID etiology
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Varies by SCID subtype, needs referral to Specialty Center
Differential Diagnosis	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.
Specific Testing Laboratories as listed in the Genetic Testing Registry	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=C0085110[DISCUI]&condition=C0085110&compare_labs=1
GeneReviews	X-SCID http://www.ncbi.nlm.nih.gov/books/NBK1410/, ADA Deficiency http://www.ncbi.nlm.nih.gov/books/NBK1483/,
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/SCID.pdf
American College of Medical Genetics Algorithm	In development
Recommended Uniform Screening Panel (RUSP)	Core

Fabry Disease
(Lysosomal Storage Disorder)

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Fabry Disease 301500 16652001/E75.21 Alpha-galactosidase A (α-Gal A) 300644 / 3.2.1.22
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Decreased α-Gal A activity 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
Diagnostic Confirmation	Deficient α-Gal A activity *GLA* mutation analysis on non-urgent basis
Differential Diagnosis	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0002986%5BDISCUI%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)

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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Gaucher Disease (GD); Glucocerebrosidase Deficiency; Glucosylceramidase Deficiency, not including Saposin C Deficiency 231000 12246008/E75.22 Glucocerebrosidase 606463/3.2.1.45
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Deficient glucocerebrosidase activity 62311-6
Initial Diagnostics at Referral Center	If no family history, repeat enzyme activity and perform *GBA* mutation analysis. If positive family history with known mutation, perform *GBA* mutation analysis.
Recommended additional testing to consider at time of initial consultation	None
Abnormal Metabolites Expected	Deficient glucocerebrosidase activity
If initial testing is negative has the disorder been ruled out?	?Yes
Diagnostic Confirmation	Deficient glucocerebrosidase activity
Differential Diagnosis	None
Specific Testing Laboratories as listed in GeneTests	http://www.ncbi.nlm.nih.gov/gtr/tests/?term=Glucosylceramidase 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 Algorithm	In development
Recommended Uniform Screening Panel (RUSP)	Not on Panel

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Coscidde* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Pompe Disease, Glycogen Storage Disease Type II (GSD II) 232300 274864009 / E74.02 Acid alpha-glucosidase (GAA) 606800 / 3.2.1.20
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Decreased GAA activity 63414-7
Initial Diagnostics at Referral Center	Leukocyte GAA activity Mutation analysis of *GAA* Determine cross-reactive immunologic material (CRIM) status Cardiac evaluation (echocardiogram (EKG))
Recommended additional testing to consider at time of initial consultation	Serum creatine kinase (CK) Urine glucose tetrasaccharide (Glc4) Alanine aminotransferase (ALT)
Abnormal Metabolites Expected	Deficient GAA activity Elevated CK Elevated Glc4 Elevated ALT
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Deficient GAA activity Known pathological mutations in trans
Differential Diagnosis	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0017921%5BDISCUI%5D&condition=C0017921&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1261/
American College of Medical Genetics ACT Sheet	www.acmg.net/StaticContent/ACT/Pompe.pdf
American College of Medical Genetics Algorithm	In development
Recommended Uniform Screening Panel (RUSP)	Core

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

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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Hurler Syndrome; Mucopolysaccharidosis, Type I (MPS I) 607014 7561003 / E76.01 α-L-iduronidase (IDUA) 252800/3.2.1.76
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Deficient IDUA 55909-6
Initial Diagnostics at Referral Center	Repeat IDUA Urine glucosaminoglycans (GAG)
Recommended additional testing to consider at time of initial consultation	Mutation analysis of IDUA
Abnormal Metabolites Expected	Increased heparin and dermatan sulfate (a GAG)
If initial testing is negative has the disorder been ruled out?	Yes
Diagnostic Confirmation	Deficient IDUA
Differential Diagnosis	None
Specific Testing Laboratories as listed in the Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0023786%5BDISCUI%5D&condition=C0023786&compare_labs=1
GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1162/
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

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

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

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

Disease (common abbreviation) *MIM #* *SNOMED Code / ICD-10-CM Code* *Enzyme or other abnormality* *MIM # / Enzyme Commission #*	Maroteaux-Lamy Syndrome; Mucopolysaccharidosis Type VI (MPS VI) 253200 69463008 / E76.29 Arylsulfatase B (ARSB) 611542 / 3.1.6.12
Abnormal Newborn Screening Metabolite(s) *LOINC Number(s)*	Deficient ARSB activity 2646-8 (Enzymatic activity, serum)
Initial Diagnostics at Referral Center	Repeat arylsulfatase B activity Urine GAG
Recommended additional testing to consider at time of initial consultation	Mutation analysis of ARSB
Abnormal Metabolites Expected	Deficient ARSB activity 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 Genetic Testing Registry	www.ncbi.nlm.nih.gov/gtr/tests/?term=C0026709%5BDISCUI%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)

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

Abbreviations

17-OHP	17-Hydroxyprogesterone
2,4Di	2,4-Dienoyl-CoA reductase deficiency
2M3HBA	2-Methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency
2MBG	2-Methylbutyryl glycinuria
3MCC	3-Methylcrotonyl-CoA carboxylase
3MGA	3-Methylglutaconic aciduria
A-Gal A	Alpha-galactosidase A
ACT sheets	Action sheets
ACTH	Adrenocorticotrophic hormone
ADA	Adenosine deaminase
α-GalA	Alpha-galactosodase A
AFP	Alpha fetoprotein
AG	Acylglycine
ALT	Alanine aminotransferase
ARG	Argininemia
ARSB	Arylsulfatase B
ASA	Argininosuccinic aciduria
ASM	Acid sphingomyelinase
B_{12}	Vitamin B_{12}, cobalamin
BAER	Brainstem auditory evoked response
BCKD	Branched-chain alpha-keto acid dehydrogenase
BIOT	Biotinidase deficiency, Biotinidase
βKT	Beta-ketothiolase deficiency
C0	Free carnitine
C10	Decanoyl carnitine
C10:1	Decenoyl carnitine
C10:2	Decadienoyl carnitine
C14	Tetradecanoyl carnitine
C14:1	Tetradecenoyl carnitine
C16	Hexadecanoyl carnitine
C16OH	Hydroxyhexadecanoyl carnitine
C18	Octadecanoyl carnitine
C18:1	Octadecenoyl carnitine
C18:1OH	Hydroxyoctadecenoyl carnitine
C2	Acetyl-L-carnitine
C22:0	Docosanoic acid
C24:0	Tetracosanoic acid
C26:0	Hexacosanoic acid
C3	Propionyl carnitine
C3DC	Malonyl carnitine
C4	Butyryl carnitine + isobutyryl carnitine
C4DC	Methylmalonyl carnitine
C4OH	Hydroxybutyryl carnitine
C5	Isovaleryl carnitine
C5:1	Tiglyl carnitine
C5DC	Glutaryl carnitine

C5OH	Hydroxyisovaleryl carnitine
C6	Hexanoyl carnitine
C6DC	Methylglutaryl carnitine
C8	Octanoyl carnitine
CACT	Carnitine-acyl carnitine translocase
CAH	Congenital adrenal hyperplasia
CBC	Complete blood count
Cbl A,B	Cobalamin A,B cofactor
Cbl C	Cobalamin C cofactor
Cbl D_1	Cobalamin D_1 cofactor
Cbl D_2	Cobalamin D_2 cofactor
Cbl F	Cobalamin F cofactor
Cbl J	Cobalamin J cofactor
CBS	Cystathionine beta-synthase
CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane receptor
CH	Congenital hypothyroidism
CIT I	Citrullinemia type I
CIT II	Citrullinemia type II
CK	Creatine kinase
CPK	Creatine phosphokinase
CPT I	Carnitine palmitoyl transferase type I deficiency
CPT II	Carnitine palmitoyl transferase type II deficiency
CRIM	Cross-reactive immunologic material
CSF	Cerebrospinal fluid
CUD	Carnitine uptake defect
EKG	Electrocardiogram
EMA	Ethylmalonic encephalopathy
FAH	Fumarylacetoacetase hydrolase
FS	Fetal and sickle cell hemoglobins
FSA	Fetal, sickle and adult hemoglobins
FSC	Fetal, sickle cell and C hemoglobins
GA 1	Glutaric acidemia type 1
GA 2	Glutaric acidemia type 2
GAA	Acid alpha-glucosidase
GAG	Glucosaminoglycans
Gal-1-P	Galactose-1-phosphate
GALC	Galactosylceraminidase
GALE	Galactose epimerase deficiency
GALK	Galactokinase
GALT	Galactose-1-phosphate uriydltransferase
GD	Gaucher disease
Glc4	Glucose tetrasaccharide
GLY	Glycine
GSD II	Glycogen storage disease, type II
HADH	Hydroxyacyl-CoA dehydrogenase
HbAS	Sickle cell carrier (adult and sickle cell hemoglobins)
HbS	Sickle cell hemoglobin
$HbSB^0$	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
PHE	Phenylalanine
PKU	Phenylketonuria
RBC	Red blood cell
RUSP	Recommended Universal Screening Panel
SA	Succinylacetone

SAA	Succinylacetoacetate
SAH	S-adenosyl homocysteine hydrolase
SCAD	Short-chain acyl-CoA dehydrogenase deficiency
SCHAD	Short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency
SCID	Severe combined immunodeficiency
SNOMED	Systematized Nomenclature of Medicine
SS	Sickle cell anemia
$SUCLA_1$	Succinate-CoA lyase, alpha subunit
$SUCLA_2$	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