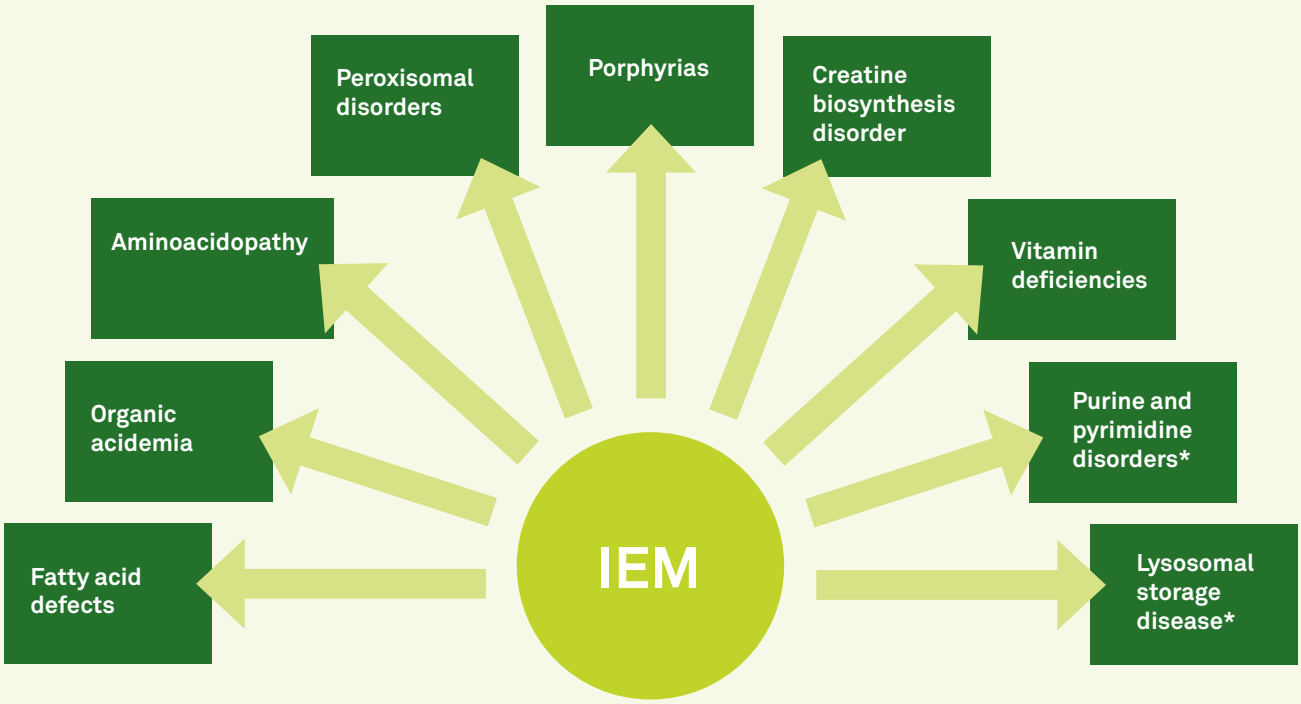
Quest Diagnostics®

Inborn errors of metabolism (IEM)

Inborn errors of metabolism (IEM) are disorders produced by a genetic defect (usually a DNA mutation) in an enzyme, transporter, chaperone molecule, or channel, resulting in the blockage of a metabolic pathway. The blockage leads to the accumulation of toxic intermediate metabolites and the deficiency of subsequent metabolites. This combination is responsible for the clinical presentation of each particular disorder.

The treatment of most IEM includes dietary restrictions and/or supplementation, which needs to be closely monitored to avoid undertreating (resulting in no clinical improvement) or overtreating the patient (producing an iatrogenic nutritional deficiency and potentially worsening the clinical presentation, or impacting proper development in pediatric cases).

Inborn errors of metabolism



* Limited test availability

Metabolic disorder	Clinical presentation in untreated patients	Some examples	Biochemical tests for diagnosis and/or surveillance
Aminoacidopathy	Symptoms range from relatively benign to severe and may include growth retardation, intellectual disability, developmental delay, learning disabilities, seizures, lethargy, coma, vomiting, metabolic acidosis or alkalosis, osteomalacia, and osteoporosis	Phenylketonuria (PKU), nonketotic hyperglycinemia (NKH), maple syrup urine disease (MSUD), tyrosinemias	Amino Acid Analysis, Plasma (767X) Amino Acid, Urine (36183X) Amino Acid, CSF (29881) Organic Acid Analysis, Urine (35819 Comprehensive or 35820 Limited)
Organic acidurias	Variable clinical manifestation, including lethargy, coma, hypotonia, seizures, ataxia, vomiting, failure to thrive, developmental delay, liver disease, neutropenia, thrombocytopenia, osteomalacia, and osteoporosis	Propionic aciduria, malonic aciduria, Mmethylmalonic acidemia, cobalamin defects, Glutaric acidurias	Acylcarnitine, Plasma (14531) Organic Acid Analysis, Urine (35819 Comprehensive) Organic Acid Analysis, Urine (35820 Limited) Methylmalonic acid (34879)
Biotinidase deficiency	Affected infants could present with episodic hypoglycemia, hypotonia, lethargy, and mild delays in development. If untreated it can lead to seizures, cutaneous abnormalities, and hearing loss	Biotinidase deficiency	Biotinidase (70132X) Biotinidase Activity with Reflex to Mutation Analysis (16537X) Biotinidase Deficiency Mutation Analysis (16526X)
Urea cycle defects	Variable clinical presentation, including failure to thrive, hyperammonemia, vomiting, seizures, lethargy, and coma	Ornithine transcarbamylase deficiency (OTC), citrullinemia type 1, argininosuccinic aciduria	Amino Acid Analysis, Plasma (767X) Amino Acid, Urine (36183X) Organic Acid Analysis, Urine (35819 Comprehensive or 35820 Limited)
Fatty acid oxidation defects	Clinical findings are variable and may include myopathy, cardiomyopathy, and hypoketotic hypoglycemia	Medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency, very long-chain acyl-coenzyme A Dehydrogenase (VLCAD) deficiency, carnitine palmitoyltransferase II deficiency (CPT II)	Acylcarnitine, Plasma (14531) Organic Acid Analysis, Urine (35819 Comprehensive or 35820 Limited) Carnitine, fractionated (70107X)
Peroxisomal disorders	Clinical symptoms vary in age of onset and severity, and may include hypotonia, dysmorphic features, neurological decompensation, skeletal abnormalities, and/or hepatic disease	Zellweger spectrum disorder, X-linked Adrenoleukodystrophy (ALD), Adrenomyeloneuropathy (AMN), Refsum disease, and racemase deficiency	Very Long Chain Fatty Acid Analysis (90559)
Congenital adrenal hyperplasia	The clinical manifestations vary with the enzyme defect and the degree of deficiency. Classical CAH may be characterized by adrenal insufficiency, salt-wasting, genital ambiguity in males (XY), and virilization of the external genitalia in females (XX)	21-hydroxylase deficiency, 17α-hydroxylase deficiency, 11β-hydroxylase deficiency	Steroid Panel, 21-Hydroxylase Deficiency/Stress (90397) Steroid Panel, Comprehensive (90392) Steroid Panel, Congenital Adrenal Hyperplasia (CAH) (90398) Steroid Panel, PCOS/CAH Differentiation (90426)
Porphyrias	Broad clinical spectrum, including neurologic symptoms and/or cutaneous photosensitivity	Acute intermittent porphyria, congenital erythropoietic porphyria, porphyria cutanea tarda, hereditary coproporphyria, variegate porphyria, and protoporphyria	Porphyrins, Fractionated, Plasma (5519) Porphyrins, Fractionated, Quantitative, 24-Hour Urine (729) Porphyrins, Fractionated, Quantitative, Random Urine (36592) Porphobilinogen, Quantitative, Random Urine (6329) Porphobilinogen, Quantitative, 24-Hour Urine (726) Delta-Aminolevulinic Acid, 24-Hour Urine (219) Delta-Aminolevulinic Acid, Random Urine (6301)
Creatine Biosynthesis disorder	In general, clinical manifestations include cognitive disability, speech and language delay, autistic-like behaviors, and epilepsy	L-arginine:glycine amidinotransferase (AGAT) deficiency, Guanidinoacetate methyltransferase (GAMT); Creatine transporter (CRTR) deficiency	Creatine Biosynthesis Disorders Panel, Urine (94600)

Biochemical Genetics Laboratory at Quest Diagnostics

Clinical Biochemical Genetics is a laboratory-based specialty of medical genetics that involves the diagnosis, evaluation, and management of patients and their families with inborn errors of metabolism (IEM). Quest Diagnostics biochemical genetics laboratory is uniquely qualified to assist families and providers with an interdisciplinary team of physicians, board-certified geneticists and genetic counselors, scientists, and laboratory technicians, all dedicated to providing quality testing with accurate and precise result interpretation and rapid turnaround time. We have over 20 years of experience in the diagnosis and follow up of patients and families with IEM.

Our expert team of board-certified geneticists and genetic counselors is available for case consultation and review. At Quest Diagnostics, we are committed to providing the latest diagnostic testing methodologies and services that can help patients find better health.

Quest Diagnostics IEM test portfolio

Quest Diagnostics offers a comprehensive biochemical genetic test menu to help with the diagnosis, treatment, and management of patients with an IEM. Assistance in test selection or interpretation of results is available from our Genetic Counselors by calling 1.866.GENE.INFO (1.866.436.3463). Additionally you may also contact the biochemical genetics laboratory directly at 1.800.642.4657 ext 4817 or ext 4423 and ask to speak with the laboratory director on call.

Test code	Test name
14531	Acylcarnitine, Plasma[1]
37735	Acylglycine, Quantitative, Urine
15340(X)	Alpha-1 Antitrypsin (AAT) Mutation Analysis[1]
17307(X)	Alpha-1 Antitrypsin (AAT) Quantitation and Mutation Analysis[1]
39521(X)	Alpha-1-Antitrypsin (AAT) Quantitation and Phenotype
235	Alpha-1 Antitrypsin, Quantitative
19779(X)	Amino Acid Analysis for MSUD, LC/MS, Plasma[1]
29881	Amino Acid Analysis, LC/MS, CSF[1]
767(X)	Amino Acid Analysis, LC/MS, Plasma[1]
36183(X)	Amino Acid Analysis, LC/MS, Urine[1]
34694	Arylsulfatase A[1]
70132(X)	Biotinidase[1]
16537(X)	Biotinidase Activity with Reflex to Mutation Analysis[1]
16526(X)	Biotinidase Deficiency Mutation Analysis[1]
14755(X)	CAH (21-Hydroxylase Deficiency) Common Mutations[1]
16072(X)	CAH (21-Hydroxylase Deficiency) Rare Mutations[1]
70107(X)	Carnitine, LC/MS/MS[1]
15948(X)	Carnitine, LC/MS/MS and Acylcarnitine[1]
90905	Canavan Disease Mutation Analysis[1]
335	Cholinesterase, Plasma
338	Cholinesterase, RBC and Plasma
37965	Cholinesterase, Serum
39481	Cholinesterase, Serum, Plasma, RBC
7961	Cholinesterase, Serum, with Dibucaine Inhibition
94600	Creatine Biosynthesis Disorders Panel, Urine[1] Includes guanidinoacetate, creatine, creatinine, and creatine/creatinine (calc).
10947(X)	Cystine, 24-Hour Urine[1]
401(X)	Cystine, Quantitative, Random Urine[1]
219	Delta Aminolevulinic Acid, 24-Hour Urine
6301	Delta Aminolevulinic Acid, Random Urine
15538(X)	Dihydropyrimidine Dehydrogenase (DPD) Gene Mutation Analysis[1]
17568	Fatty Acid Panel, Comprehensive (C8-C26), Serum[1]
11254	Fatty Acid Panel, Essential[1]
94823	Fatty Acid Panel, Mitochondrial (C8-C18), Serum[1]
16613(X)	Galactosemia Mutation Analysis[1]
90907	Gaucher Disease, DNA Mutation Analysis[1]
500	Glucose-6-Phosphate Dehydrogenase, Quantitative
90915	Glycogen Storage Disease Type Ia Mutation Analysis (Ashkenazi Jewish)[1]
16612	HEXA Mutation Analysis, Gene Sequencing[1] Includes sequencing of the entire coding region, the intron-exon splice sites, and the promoter region of the HEXA gene. Consider common mutation testing (Tay-Sachs Disease Mutation Analysis) prior to, or concurrently with, this test. Hexosaminidase testing should also be considered before or concurrently with this test.
31789	Homocysteine
523(X)	5-Hydroxyindoleacetic Acid (5-HIAA), 24-Hour Urine[1]
39625(X)	5-Hydroxyindoleacetic Acid (5-HIAA), 24-Hour Urine, with Creatinine[1]
1648(X)	5-Hydroxyindoleacetic Acid (5-HIAA), Random Urine[1]
11244	Long Chain Acyl-CoA Dehydrogenase (LCHAD) Mutation Analysis[1]

Test code	Test name
36455	Lysosomal Acid Lipase Activity, Blood
90909	Maple Syrup Urine Disease (MSUD) Mutation Analysis (Ashkenazi Jewish)[1]
91284	Medium Chain Acyl-CoA Dehydrogenase (MCAD) Gene Sequencing[1]
11176(X)	Medium Chain Acyl-CoA Dehydrogenase (MCAD) Mutation Analysis[1]
34879	Methylmalonic Acid[1]
91003	Methylmalonic Acid and Homocysteine[1]
91032	Methylmalonic Acid, GC/MS/MS, Urine[1]
90899	Mucolipidosis Type IV Mutation Analysis[1]
90893	Niemann-Pick Disease Mutation Analysis[1]
35819	Organic Acids, Comprehensive, Quantitative, Urine[1]
35820	Organic Acids, Limited, Quantitative, Urine[1]
38684	Orotic acid, Urine
37356	Phenylalanine[1]
26336	Phenylalanine and Tyrosine[1]
16152(X)	Phenylketonuria (PKU) Mutation Analysis[1]
726	Porphobilinogen, Quantitative, 24-Hour Urine[1]
6329	Porphobilinogen, Quantitative, Random Urine
5519	Porphyrins, Fractionated, Plasma[1]
17198	Porphyrins, Fractionated, Quantitative and Porphobilinogen, 24-Hour Urine[1]
729	Porphyrins, Fractionated, Quantitative, 24-Hour Urine[1]
36592	Porphyrins, Fractionated, Quantitative, Random Urine[1]
10290	Porphyrins, Total, Plasma[1]
90392	Steroid Panel, Comprehensive[1] Includes androstenedione (17182), corticosterone (6547X), cortisol (11281), cortisone (37098X), deoxycorticosterone (90973), 11-deoxycortisol (30543), DHEA (19894), 18-hydroxycorticosterone (94621), 17-hydroxypregnenolone (8352), 17-hydroxyprogesterone (17180), pregnenolone (31493X), progesterone (17183), and total testosterone (15983).
90398	Steroid Panel, Congenital Adrenal Hyperplasia (CAH)[1] Includes androstenedione (17182), cortisol (11281), deoxycorticosterone (90973), 11-deoxycortisol (30543), DHEA (19894), 17-hydroxypregnenolone (8352), 17-hydroxyprogesterone (17180), progesterone (17183), and total testosterone (15983).
90397	Steroid Panel, 21-Hydroxylase Deficiency/Stress[1] Includes 17-hydroxyprogesterone (17180), androstenedione (17182), and cortisol (11281).
90426	Steroid Panel, PCOS/CAH Differentiation[1] Includes 11-deoxycortisol (30543), 17-hydroxyprogesterone (17180), androstenedione (17182), DHEA (19894), and total and free testosterone (36170).
90903	Tay-Sachs Disease Mutation Analysis[1] Includes HEXA gene analysis for 1278insTATC, delta7.6kb, G269S, IVS9+1G>A, IVS12+1G>C, and R178H mutations and the R247W pseudodeficiency allele. Consider hexosaminidase enzyme carrier screening before or concurrently with this test.
959	Tryptophan, LC/MS[1]
902	Tyrosine[1]
90559	Very Long Chain Fatty Acids[1]
39517(X)	VMA (Vanillylmandelic Acid), 24-Hour Urine[1]
934(X)	VMA (Vanillylmandelic Acid), 24-Hour Urine without Creatinine[1]
1710	VMA (Vanillylmandelic Acid), Random Urine[1]

[1] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the US Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

Reflex tests are performed at an additional charge. Panel components may be ordered separately. Multiple test codes are available. Refer to the Quest Diagnostics Directory of Services or the online Test Center (QuestDiagnostics.com) for test information.

Quest Diagnostics®

Why choose Quest Diagnostics?

Expertise
Quest Diagnostics provides you with timely access to vital information you need to help you improve the health of your patients. With more than 600 medical and scientific experts on staff, Quest Diagnostics can quickly connect you with the information and insights you and your patients need. Our consultative network for genetics is comprised of board-certified geneticists and genetic counselors with extensive experience.

Comprehensive menu of specialized tests
Because we know you want to do your very best for each of your patients, our broad array of services and comprehensive menu of specialized tests was designed with you and your patients' needs in mind. Every year, new advanced tests are developed through rigorous clinical studies using cutting-edge technology. Much of this work is done at Quest Diagnostics Nichols Institute, a world-class research institute focusing on innovative diagnostic testing.

Advocates better health in the care continuum
With information and insights accessible to physicians and patients alike, Quest Diagnostics can help you and your patients work together towards better health. The easy access offered by our more than 2,200 patient service centers (PSCs) nationwide makes it simple and convenient for patients to get the tests they need from screening and diagnosis to prognosis, treatment, and monitoring. Quest Diagnostics offers patients convenient, easy access to test results through MyQuest™. Through the MyQuest patient portal, patients get valuable insights into their personal health. They can access lab results on their computer, tablet, or smartphone, manage medications, and share health information with physicians and other healthcare professionals. Quest Diagnostics promotes patient engagement—an engaged patient is a healthier patient.

Publications

Our team of medical and laboratory experts remain active in publishing and advancing the latest thinking in metabolic disorders.

Articles:

Guerrero RB, Salazar D, Tanpaiboon P. Laboratory diagnostic approaches in metabolic disorders. *Ann Transl Med.* 2018;6(24):470. doi: 10.21037/atm.2018.11.05

Leydiker KB, Neidich JA, Lorey F, et al. Maternal medium-chain acyl-CoA dehydrogenase deficiency identified by newborn screening. *Mol Genet Metab.* 2011;103(1):92-95. doi: 10.1016/j.ymgme.2011.01.011

Park NJ, Morgan C, Sharma R, et al. Improving accuracy of Tay Sachs carrier screening of the non-Jewish population: analysis of 34 carriers and six late-onset patients with HEXA enzyme and DNA sequence analysis. *Pediatr Res.* 2010;67(2):217-220. doi: 10.1203/PDR.0b013e3181c6e318

Guerrero RB, Wolfe LA, Payne N, et al. Essential fatty acid profiling for routine nutritional assessment unmasks adrenoleukodystrophy in an infant with isovaleric acidaemia. *J Inherit Metab Dis.* 2008;31(2):S453-456. doi: 10.1007/s10545-008-1039-y

Books:

Sarafoglou K, Hoffman G, Roth K. Pediatric Endocrinology and Inborn Errors of Metabolism, Second Edition. New York, NY: McGraw Hill Education; 2017.

Poster/Abstracts:

Sharma R, Tanpaiboon P, Kucera C, Epstein BK, Taylor JC, Lacbawan FL, Salazar D. Diagnosis of porphyrias by urine and plasma fractionated porphyrins: experience at biochemical genetics laboratory, Quest Diagnostics. Poster presentation scheduled: 42nd Annual Meeting of the Society for Inherited Metabolic Disorders; April 26-29, 2020; Austin, TX. [Conference cancelled.]

Tanpaiboon P, Sharma R, Kucera C, Salazar D. L-Alloisoleucine levels in a case series of patients with isovaleric acidemia. Poster presented at: Annual Clinical Genetics Meeting Digital Edition of The American College of Medical Genetics and Genomics; May 1, 2020.

Sharma R, Salazar D, Davoodi-Semiromi A, Guerrero RB, Buller-Burckle A, Lobo RM, Beierle R, Neidich JA, Lacbawan FL, Tanpaiboon P. Biotinidase biochemical and molecular analyses: experience at Quest Diagnostics Nichols Institute biochemical genetics laboratory. Poster presented at the 41st Annual Meeting of the Society for Inherited Metabolic Disorders; April 6-9, 2019; Bellevue, WA.

Salazar D, Goldman S, Weber D, Ross J, Albi S, Patrimonio L, Albi A, Sharma R, Davoodi R, Guerrero RB, Boktor J, Lacbawan FL, Tanpaiboon P, Clarke N. A new method for automated solid phase extraction of organic acids in urine followed by gas chromatography –time of flight mass spectrometry (GC/Q-TOF) analysis. Poster presented at the 41st Annual Meeting of the Society for Inherited Metabolic Disorders; April 6-9, 2019; Bellevue, WA.

Sharma R, Tanpaiboon P, Salazar D, Guerrero RB, Lacbawan FL. Diagnosis of fatty acid oxidation disorders: experience at Quest Diagnostics Nichols Institute biochemical genetics laboratory. Poster presented at the 2018 symposium for the International Network for Fatty Acid Oxidation Research and Management (INFORM); September 2-3, 2018; Athens, Greece.

Sharma R, Salazar D, Guerrero RB, Davoodi-Semiromi A, Lacbawan FL. Diagnosis of peroxisomal storage disorders by very long chain fatty acids analysis: experience at Quest Diagnostics Nichols Institute biochemical genetics laboratory. Poster presented at the 13th International Congress of the Society for the Study of Inborn Errors of Metabolism; September 5-8, 2017; Rio de Janeiro, Brazil.

Sharma R, Salazar, D, Guerrero RB, Davoodi-Semiromi A, Lobo RM, Zhang K, Lee LE, Neidich JA, Strom CM. 15 years' experience: diagnosis of organic acidemias at Quest Diagnostics biochemical genetics laboratory. Poster presented at the Annual Symposium of the Society for the Study of Inborn Errors of Metabolism; September 6-9, 2016; Rome, Italy.

Sharma R, Salazar D, Carlton E, Guerrero RB, Strom CM, Neidich JA. Quantitative urine organic acids reference ranges in pediatric and adult age groups. Poster presented at the 33rd Annual Meeting of the Society of Inherited Metabolic Disorders; March 27-31, 2010; Albuquerque, NM.

Call our team of genetic counselors at 1.866.GENE.INFO (1.866.436.3463) for specific test information or a clinical consultation. Additionally you may also contact the biochemical genetics laboratory directly at 1.800.642.4657 ext 4817 or ext 4423 and ask to speak with the laboratory director on call.

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