

Developmental Delay/Mental Retardation (DD/MR)

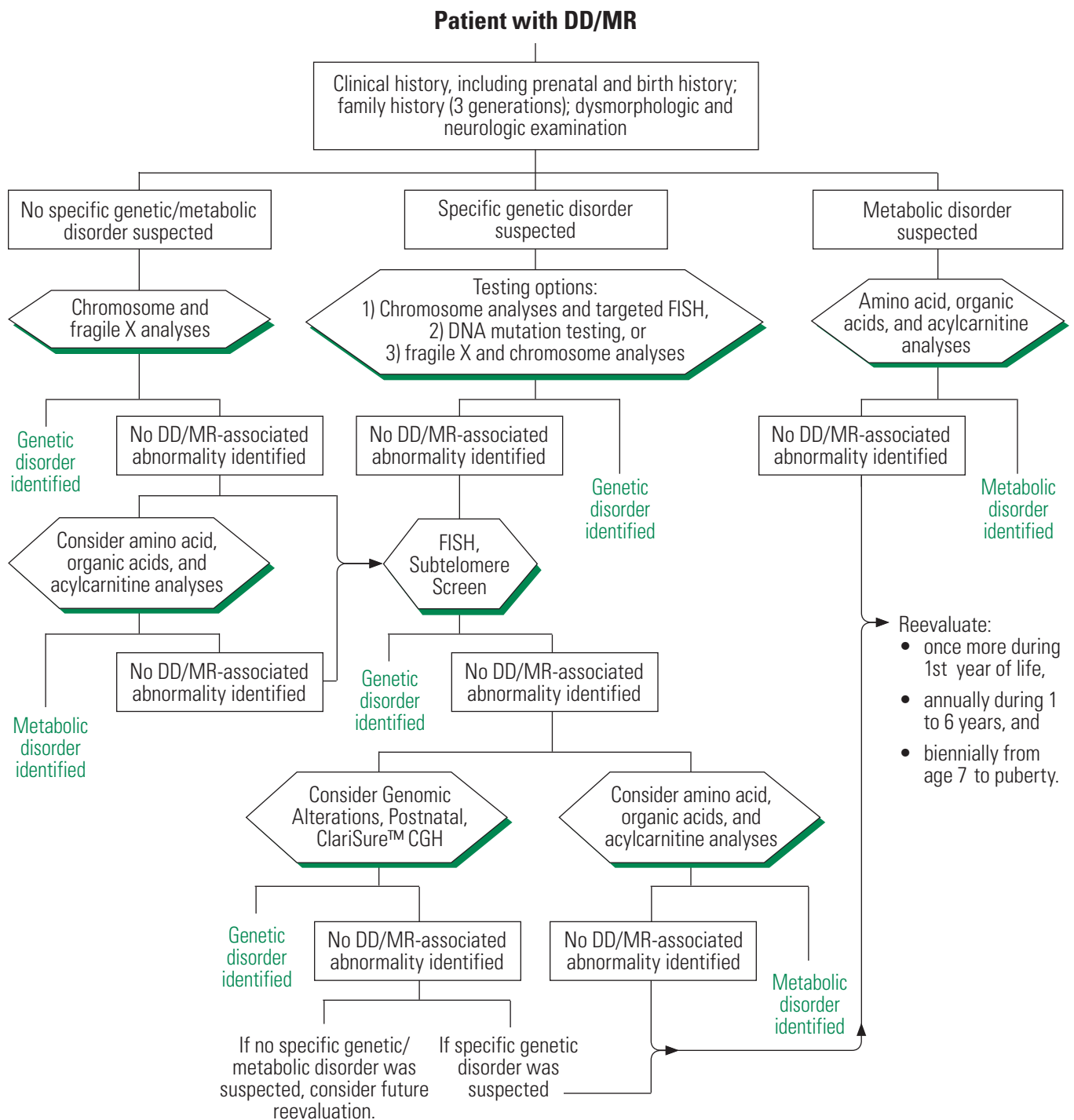


Figure. Laboratory evaluation of developmental delay/mental retardation. The algorithm is intended to assist in diagnosis of DD/MR and is based in part on information published in references 1-3. CGH, comparative genomic hybridization.

Test Menu and Clinical Application

Individuals who present with DD/MR may benefit from the tests listed below. Some patients not yet diagnosed with DD/MR may manifest other symptoms suggestive of a genetic or metabolic disorder. These symptoms are presented herein to help identify patients who may benefit from a specific test.

Acylcarnitine, Plasma

Test Code: 14531X

Clinical Use: Diagnose organic aciduria or fatty acid disorder

Individuals Suitable for Testing: Those with cardiac arrhythmia, marked hypoglycemia, hepatomegaly, seizures, coma, muscle disease, lethargy

Specimen Requirements: 1 mL frozen plasma (sodium heparin, green-top tube); 0.2 mL minimum

CPT Code^a: 82017

Amino Acid Analysis for MSUD, LC/MS, Plasma

Test Code: 19779X

Clinical Use: Diagnose maple syrup urine disease (MSUD); monitor branched chain amino acid levels in patients with MSUD

Individuals Suitable for Testing: Those with seizures, alternating hypertonia/hypotonia, poor feeding, lethargy, failure to thrive; those diagnosed with MSUD

Specimen Requirements: 2 mL frozen plasma (sodium heparin, green-top tube); 0.25 mL minimum

CPT Code^a: 82136

Amino Acid Analysis, LC/MS, CSF

Test Code: 29881X

Clinical Use: Diagnose amino acid disorders in which CSF levels are elevated relative to other sample types (eg, nonketotic hyperglycinemia)

Individuals Suitable for Testing: Those with convulsions, apnea, hypotonia, poor feeding, wandering eye movements, muscle spasms, lethargy, hiccups

Specimen Requirements: 1 mL frozen CSF; 0.25 mL minimum

CPT Code^a: 82139

Amino Acid Analysis, LC/MS, Plasma

(Includes 34 analytes)

Test Code: 767X

Clinical Use: Diagnose primary aminoacidopathies or screen for secondary aminoacidopathies; monitor response to therapy

Individuals Suitable for Testing: Those with variable symptoms that may include coma, seizures, tachypnea, poor feeding, failure to thrive, vomiting, lethargy; those diagnosed with aminoacidopathy

Specimen Requirements: 2 mL frozen plasma (sodium heparin, green-top tube); 0.25 mL minimum

CPT Code^a: 82139

Amino Acid Analysis, Limited, LC/MS, Plasma

(Includes 6 amino acids associated with the most common aminoacidopathies)

Test Code: 1776X

Clinical Use: Diagnose primary aminoacidopathies or screen for secondary aminoacidopathies; monitor response to therapy

Individuals Suitable for Testing: Those with variable symptoms that may include coma, seizures, tachypnea, poor

feeding, failure to thrive, vomiting, lethargy; those diagnosed with aminoacidopathy

Specimen Requirements: 2 mL frozen plasma (sodium heparin, green-top tube); 0.25 mL minimum

CPT Code^a: 82139

Amino Acid Analysis, LC/MS, Urine

(Includes creatinine)

Test Code: 36183X

Clinical Use: Diagnose primary and secondary aminoacidopathies

Individuals Suitable for Testing: Those with variable symptoms that may include coma, seizures, tachypnea, poor feeding, failure to thrive, vomiting, lethargy

Specimen Requirements: 2 mL frozen random urine; 0.5 mL minimum

Plasma is preferred over urine except when abnormalities are more likely to manifest in urine (eg, arginosuccinic acid lyase deficiency, disorders of transsulfuration/amino acid transport)

CPT Codes^a: 82139; 82570

Canavan Disease Mutation Analysis^b

Test Code: 31650X

Clinical Use: Diagnose Canavan disease; determine carrier status

Individuals Suitable for Testing: Those with seizures, spasticity, poor visual fixation, irritability, poor feeding, poor head control, hypotonia, increased deep tendon reflexes, increased head circumference, or a family history of Canavan disease

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube); 3 mL minimum

CPT Codes^a: 83891; 83892; 83896 (x8); 83900; 83901; 83909; 83912; 83914 (x4)

Carnitine, LC/MS/MS

(Includes free and total carnitine and carnitine esters)

Test Code: 30299X

Clinical Use: Diagnose primary or secondary carnitine deficiency; monitor patients with carnitine deficiency

Individuals Suitable for Testing: Those with tachycardia, hepatomegaly, hypotonia, lethargy; those diagnosed with carnitine deficiency

Specimen Requirements: 1 mL frozen serum; 0.4 mL minimum

CPT Code^a: 82379

Carnitine, LC/MS/MS and Acylcarnitine

Test Code: 15948X

Clinical Use: Diagnose organic aciduria, fatty acid disorder, primary or secondary carnitine deficiency

Individuals Suitable for Testing: Those with cardiac arrhythmia or tachycardia, hepatomegaly, seizures, hypotonia, coma, lethargy

Specimen Requirements: 2 mL frozen plasma (sodium heparin, green-top tube); 0.6 mL minimum

CPT Codes^a: 82379; 82017

Chromosome Analysis, Blood

Test Code: 14596X

Clinical Use: Determine genetic cause of DD/MR

Individuals Suitable for Testing: Those with dysmorphic features, birth defects, growth abnormalities, behavior problems

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88230; 88262; 88291

Chromosome Analysis, Follow-up

Test Code: 10708X

Clinical Use: Diagnose a chromosomal abnormality

Individuals Suitable for Testing: Family members of individuals with a known chromosomal abnormality

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88230; 88262; 88291

Chromosome Analysis, High Resolution

Test Code: 14595X

Clinical Use: Diagnose DD/MR associated with small chromosomal deletions, duplications, or rearrangements

Individuals Suitable for Testing: Those with DD/MR being evaluated for subtle chromosomal abnormalities not identifiable by routine chromosome analysis

Specimen Requirements: 10 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88230; 88262; 88289; 88291

FISH, Angelman^b

Test Code: 14608X

Clinical Use: Diagnose Angelman syndrome

Individuals Suitable for Testing: Those with seizures, wide mouth, protruding tongue, prominent jaw, thin upper lip, absent speech, ataxic gait, paroxysmal laughter, light hair/skin pigmentation

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271; 88273; 88291

FISH, Cri du chat^b

Test Code: 14614X

Clinical Use: Diagnose Cri du chat syndrome

Individuals Suitable for Testing: Those with cat-like cry, severe psychomotor dysfunction, microencephaly, round face, hypertelorism, small jaw, low-set ears, epicanthal folds, hypotonia

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271; 88273; 88291

FISH, DiGeorge, Velocardiofacial (VCFS)^b

Test Code: 14610X

Clinical Use: Diagnose DiGeorge/velocardiofacial syndrome

Individuals Suitable for Testing: Those with cardiac malformations, seizures, hypocalcemia, high susceptibility to infections, hypertelorism, cleft palate, bifid uvula, small jaw, low-set ears, speech delay, scoliosis, hernia, schizophrenia/mental health disorders

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271; 88273; 88291

FISH, Miller-Dieker^b

Test Code: 14612X

Clinical Use: Diagnose Miller-Dieker syndrome

Individuals Suitable for Testing: Those with central nervous system disorders, microencephaly/lissencephaly, prominent forehead, bitemporal hollowing, small nose with upturned nares, protuberant upper lip, thin vermilion border of upper lip

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271; 88273; 88291

FISH, Smith-Magenis^b

Test Code: 14611X

Clinical Use: Diagnose Smith-Magenis syndrome

Individuals Suitable for Testing: Those with heart defect, brachycephaly, hearing loss, speech delay with hoarse/deep voice, sleep disturbance, hyperactivity, self-destructive behavior, broad face/ nasal bridge, Down syndrome-like facies

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271; 88273; 88291

FISH, Microdeletion Syndromes Panel^b

Test Code: 37559X

Clinical Use: Diagnose Angelman, DiGeorge, Kallmann, Prader-Willi, Smith-Magenis, and Williams syndromes

Individuals Suitable for Testing: Those with symptoms associated with microdeletion syndromes

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271 (x4); 88273; 88291

FISH, Neonatal Screen

Test Code: 36053X

Clinical Use: Determine genetic cause of DD/MR (includes +13, +18, +21, X, Y)

Individuals Suitable for Testing: Those with dysmorphic features, birth defects, growth abnormalities, behavior problems

Specimen Requirements: 3 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271 (x5); 88275; 88291

FISH, Subtelomere Screen^b

Test Code: 10468X

Clinical Use: Determine genetic cause of DD/MR

Individuals Suitable for Testing: Those with negative chromosome, fragile X analyses whose phenotype remains suspicious for a genetic abnormality

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 3 mL minimum

CPT Codes^a: 88271 (x41); 88272 (x15); 88291

FISH, Wolf-Hirschhorn^b

Test Code: 14613X

Clinical Use: Diagnose or confirm the diagnosis of Wolf-Hirschhorn syndrome

Individuals Suitable for Testing: Those with cardiac septal defects, microcephaly, hypotonia, seizures, hypospadias/cryptorchidism (males), absent uterus (females), prominent glabella, short philtrum, hypertelorism, downturned corners of mouth

Specimen Requirements: 5 mL room temperature whole blood (sodium heparin, green-top tube); 2 mL minimum

CPT Codes^a: 88271; 88273; 88291

Fragile X with Reflex^{c,d}

Test Code: 19757X

Clinical Use: Diagnose fragile X syndrome; determine carrier status

Individuals Suitable for Testing: Those with dysmorphic features, birth defects, growth abnormalities, behavior problems, or at risk of carrying fragile X abnormality

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube); 3 mL minimum

CPT Codes^a: 83891; 83894; 83900; 83909; 83912

Fragile X with Reflex^{c,d} and Chromosome Analysis, Blood

Test Code: 19792X

Clinical Use: Determine genetic cause of DD/MR; diagnose fragile X syndrome; determine fragile X carrier status

Individuals Suitable for Testing: Those with dysmorphic features, birth defects, growth abnormalities, behavior problems, or at risk of carrying fragile X abnormality

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube, 5 mL minimum) AND 5 mL room temperature whole blood (sodium heparin, green-top tube, 2 mL minimum)

CPT Codes^a: 83891; 83894; 83900; 83909; 83912; 88230; 88262; 88291

Gaucher Disease, DNA Mutation Analysis^b

Test Code: 21503X

Clinical Use: Diagnose Gaucher disease; determine carrier status

Individuals Suitable for Testing: Those with hepatosplenomegaly, bone fractures and lesions, thrombocytopenia, or a family history of Gaucher disease

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube); 3 mL minimum

CPT Codes^a: 83891; 83892; 83896 (x16); 83900; 83909; 83912; 83914 (x8)

Genomic Alterations, Postnatal, ClariSure™ CGH^b

Test Code: 16135X

Clinical Use: Determine genetic cause of DD/MR

Individuals Suitable for Testing: Those with negative chromosome, fragile X, and subtelomeric FISH analyses

Specimen Requirements: 10 mL room temperature whole blood (sodium heparin, green-top tube); 5 mL minimum

CPT Codes^a: 88386; 83891; 83892; 83898

Homocysteine (Nutritional and Congenital), Serum

Test Code: 36362X

Clinical Use: Diagnose homocystinuria; monitor homocysteine levels in patients with homocystinuria

Individuals Suitable for Testing: Those with dislocated ocular lens, osteoporosis, scoliosis, thinning/lengthening of long bones, thromboembolism, psychiatric disorders, or diagnosed homocystinuria

Specimen Requirements: 1 mL refrigerated serum (red-top tube); 0.5 mL minimum

CPT Code^a: 83090

Maple Syrup Disease (MSUD) Mutational Analysis (Ashkenazi Jewish)^b

Test Code: 16067X

Clinical Use: Diagnose MSUD; determine carrier status

Individuals Suitable for Testing: Those with seizures, alternating hypertonia/hypotonia, poor feeding, lethargy, failure to thrive, or a family history of MSUD

Specimen Requirements: 5 mL refrigerated whole blood (EDTA, lavender-top tube); 3 mL minimum

CPT Codes^a: 83891; 83892 (x2); 83909; 83900; 83901; 83914 (x3); 83912

Methylmalonic Acid

Test Code: 34879X

Clinical Use: Diagnose methylmalonic acidemia; monitor methylmalonic acid levels after diagnosis

Individuals Suitable for Testing: Those with respiratory distress, hepatomegaly, lethargy, failure to thrive, vomiting, hypotonia, or with diagnosed methylmalonic acidemia

Specimen Requirements: 2 mL refrigerated serum (red-top tube); 0.6 mL minimum

CPT Code^a: 83921

Methylmalonic Acid, Urine

(Includes creatinine)

Test Code: 34877X

Clinical Use: Diagnose methylmalonic acidemia; monitor methylmalonic acid levels after diagnosis

Individuals Suitable for Testing: Those with respiratory distress, hepatomegaly, lethargy, failure to thrive, vomiting, hypotonia, or with diagnosed methylmalonic acidemia

Specimen Requirements: 5 mL frozen random urine; 1 mL minimum

CPT Codes^a: 82570; 83921

Niemann-Pick Disease Mutation Analysis^b

Test Code: 10222X

Clinical Use: Diagnose Niemann-Pick disease; determine carrier status

Individuals Suitable for Testing: Those with hepatosplenomegaly, hypotonia, muscle weakness, vomiting, constipation, cherry-red corneal spot, or with a family history of Niemann-Pick disease

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube); 3 mL minimum

CPT Codes^a: 83891; 83892; 83896 (x8); 83900; 83909; 83912; 83914 (x4)

Organic Acids, Qualitative, Urine

Test Code: 10049X

Clinical Use: Screen for organic aciduria

Individuals Suitable for Testing: Those with variable symptoms that may include coma, liver disease, seizures, hypotonia, ataxia, failure to thrive, lethargy

Specimen Requirements: 15 mL frozen random urine; 5 mL minimum

CPT Code^a: 83919

Organic Acids, Quantitative, Random Urine, Full Panel

Test Code: 38067X

Clinical Use: Diagnose organic aciduria

Individuals Suitable for Testing: Those with variable symptoms that may include coma, liver disease, seizures, hypotonia, ataxia, failure to thrive, lethargy

Specimen Requirements: 15 mL frozen random urine; 5 mL minimum

CPT Code^a: 83918

Phenylalanine

Test Code: 37356X

Clinical Use: Diagnose phenylketonuria; monitor phenylalanine levels after diagnosis

Individuals Suitable for Testing: Those with seizures, poor feeding, vomiting, hyperactivity, eczema, hypopigmentation; those diagnosed with phenylketonuria

Specimen Requirements: 0.4 mL frozen plasma (sodium heparin, green-top tube); 0.2 mL minimum

CPT Code^a: 84030

Prader-Willi/Angelman Syndrome^b

Test Code: 11369Z

Clinical Use: Diagnose Prader-Willi or Angelman syndrome

Individuals Suitable for Testing: Those with severe hypotonia, poor feeding leading to gavage feeding, cryptorchidism (males), hypoplastic labia (females), strabismus, narrow bitemporal diameter, upslanting fissures, short stature, small hands and feet, obesity, hyperphagia, ataxic gate, paroxysmal laughter

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube); 3 mL minimum

CPT Codes^a: 83891; 83892; 83894 (x2); 83900; 83912

Rett Syndrome Mutation Analysis^b

Test Code: 15088X

Clinical Use: Diagnose Rett syndrome

Individuals Suitable for Testing: Males with unexplained neonatal encephalopathy; those with Angelman-type symptoms with normal chromosome 15q11.2-q13; or those

with X-linked mental retardation and a negative fragile X test

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube); 2 mL minimum

CPT Codes^a: 83891; 83892; 83909; 83898 (x6); 83904 (x5); 83912

Tay-Sachs Disease Mutation Analysis^b

Test Code: 21502X

Clinical Use: Diagnose Tay-Sachs disease; determine carrier status

Individuals Suitable for Testing: Those with macular pallor with cherry red spot, blindness, dementia, apathy; family members at risk of carrying a Tay-Sachs mutation

Specimen Requirements: 5 mL room temperature whole blood (EDTA, lavender-top tube); 3 mL minimum

CPT Codes^a: 83891; 83892; 83896 (x14); 83900; 83901 (x2); 83909; 83912; 83914 (x7)

Tryptophan, LC/MS

Test Code: 959X

Clinical Use: Diagnose tryptophanuria; monitor tryptophan levels after diagnosis

Individuals Suitable for Testing: Those with photosensitive skin rash, short stature, cerebellar-like ataxia; those diagnosed with tryptophanuria

Specimen Requirements: 2 mL frozen plasma (sodium heparin, green-top tube); 0.25 mL minimum

CPT Code^a: 82131

Tyrosine

Test Code: 902X

Clinical Use: Diagnose tyrosinemia; monitor tyrosine levels after diagnosis

Individuals Suitable for Testing: Those with liver disease, eye symptoms of lacrimation, photophobia, redness, pain; nonpruritic, painful hyperkeratotic skin lesions; those with diagnosed tyrosinemia

Specimen Requirements: 0.4 mL frozen plasma (sodium heparin, green-top tube); 0.2 mL minimum

CPT Code^a: 84510

Phenylalanine and Tyrosine

Test Code: 26336X

Clinical Use: Monitor response to treatment of phenylketonuria

Individuals Suitable for Testing: Those with diagnosed phenylketonuria

Specimen Requirements: 0.4 mL frozen plasma (sodium heparin, green-top tube); 0.2 mL minimum

CPT Codes^a: 84030; 84510

^aThe CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payor being billed.

^bThis test was developed and its performance characteristics have been determined by Quest Diagnostics Nichols Institute. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. Performance characteristics refer to the analytical performance of the test.

^cReflex tests are performed at an additional charge and are associated with additional CPT codes. For males, if PCR result suggests carrier status, an abnormal result, or no *FMRI* amplification product, then Southern blot is performed. For females, if PCR result suggests carrier status, normal homozygous *FMRI* alleles, or gray zone, then capillary electrophoresis Southern analysis (CSA) is performed; abnormal CSA results are followed-up with Southern blot.

^dThis test was developed and its performance characteristics have been determined by Quest Diagnostics Nichols Institute. Performance characteristics refer to the analytical performance of the test.

References

1. Curry CJ, Stevenson RE, Aughton D, et al. Evaluation of mental retardation: recommendations of a consensus conference. *Am J Med Genetics*.1997;72:468-477.
2. Shaffer LG. American College of Medical Genetics guideline on the cytogenetic evaluation of the individual with developmental delay or mental retardation. *Genet Med*. 2005;7:650-654.
3. Sherman S, Pletcher BA, Driscoll DA. Fragile X syndrome: diagnostic and carrier testing. *Genet Med*. 2005;7:584-587.

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