MAYO CLINIC LABORATORIES

Test Definition: PDHC

Pyruvate Dehydrogenase Complex, Fibroblasts

Overview

Useful For

Evaluation of patients with a clinical suspicion of a pyruvate dehydrogenase complex deficiency or an energy metabolism disorder

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No

Genetics Test Information

Pyruvate dehydrogenase complex (PDHC) deficiency is a rare mitochondrial disorder with a clinical presentation consisting of metabolic and neurological components of varying severity.

PDHC should be considered in patients with early-onset neurological disease and unexplained lactic acidosis, especially if structural brain abnormalities are present.

Testing Algorithm

When this test is ordered, a fibroblast culture will always be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Special Instructions

- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Method Name

PDHC: Colorimetric Enzyme Assay
CULFB: Cell Culture

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test is not available for prenatal testing.

This assay is intended as a screening test to detect decreases in total pyruvate dehydrogenase complex (PDHC) activity and is used for the evaluation of patients with a clinical suspicion of a PDHC deficiency or an energy metabolism disorder. It is not designed to detect cases of pyruvate dehydrogenase (PDH) kinase or phosphatase deficiencies. Additional molecular or enzymatic testing is necessary to determine the specific defect in the PDHC; call 800-533-1710 for testing options.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Cultured fibroblasts
Container/Tube: T-75 or T-25 flask
Specimen Volume: 1 Full T-75 flask or 2 full T-25 flasks
Specimen Stability Information: Ambient (preferred)/Refrigerated <24 hours

Specimen Type: Skin biopsy
Supplies: Fibroblast Biopsy Transport Media (T115)
Container/Tube: Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin. Tubes can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin).
Specimen Volume: 4-mm punch
Specimen Stability Information: Refrigerated (preferred)/Ambient

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Reject Due To

Tissue in formalin or fixative preservative	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Varies		

Clinical & Interpretive

Clinical Information

The pyruvate dehydrogenase (PDH) complex (PDHC) catalyzes the oxidative decarboxylation of pyruvate to acetyl-CoA, a

critical step in the production of cellular energy. PDHC is a multienzyme complex located in the inner mitochondrial membrane consisting of 6 different components: pyruvate decarboxylase (E1, with alpha and beta subunits), dihydrolipoic transacetylase (E2), dihydrolipoyl dehydrogenase (E3), 2 regulatory enzymes (PDH kinase and PDH phosphatase), and E3-binding protein.

PDHC deficiency is a mitochondrial disorder with a variable clinical presentation ranging from fatal congenital lactic acidosis to relatively mild ataxia or neuropathy. In infants and children with PDHC deficiency, the most common features are delayed development and hypotonia, as well as acquired microcephaly. Seizures and ataxia are also frequent features. Less common manifestations include congenital brain malformations, particularly ventriculomegaly and agenesis of the corpus callosum, or degenerative changes including Leigh disease. Facial dysmorphism is seen in a small portion of patients. PDHC deficiency is one of the most common causes of primary lactic acidosis in children. The severity of the disease progression is thought to be related to the severity of the lactic acidosis as well as the level of residual enzyme activity.

PDHC deficiency can be caused by defects in the E1 alpha, E1 beta, E2, or E3 subunits. The most common cause of PDHC deficiency is a defect in the E1 alpha subunit, which is encoded by the *PDH1* gene located on the X chromosome. Both females and males with a *PDH1* gene mutation are affected with PDHC deficiency; thus, it is classified as X-linked dominant. Mutations in the *PDH1* gene are typically de novo.

A major cause of primary lactic acidosis in children is PDHC deficiency; therefore, it should be suspected when blood and cerebrospinal fluid (CSF) lactate and pyruvate is elevated and the lactate-to-pyruvate (L:P) ratio is normal or slightly elevated. Plasma or CSF alanine (AAQP / Amino Acids, Quantitative, Plasma or AACSF / Amino Acids, Quantitative, Spinal Fluid) may also be increased.

A diagnosis of PDHC deficiency depends on the measurement of enzyme activity in cells or tissues, most commonly in skin fibroblasts.

Reference Values

>25.00 nmol/min/g protein (Normal)
5.00-25.00 nmol/min/g protein (Indeterminate)
<5.00 nmol/min/g protein (Deficient)
Reference values apply to all ages.

Interpretation

When below-normal enzyme activities are detected, a detailed interpretation is given. This interpretation includes an overview of the results and their significance, a correlation to available clinical information, elements of differential diagnosis, and recommendations for additional biochemical testing.

Cautions

No significant cautionary statements

Clinical Reference

1. Patel KP, O'Brien TW, Subramony SH, Shuster J, Stacpoole PW: The spectrum of pyruvate dehydrogenase complex deficiency: clinical, biochemical and genetic features in 371 patients. Mol Genet Metab. 2012 Jul;106(3):385-394. doi: 10.1016/j.ymgme.2011.09.032
2. Robinson BH: Lactic Acidemia: Disorders of Pyruvate Carboxylase and Pyruvate Dehydrogenase. In: Valle DL,

Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed October 12, 2022. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225087140

3. Lib M, Rodriguez-Mari A, Marusich MF, Capaldi RA: Immunocapture and microplate-based activity measurement of mammalian pyruvate dehydrogenase complex. Anal Biochem. 2003 Mar 1;314(1):121-127. doi: 10.1016/s0003-2697(02)00645-0.PMID:12633610

4. Shin HK, Grahame G, McCandless SE, Kerr DS, Bedoyan JK: Enzymatic testing sensitivity, variability and practical diagnostic algorithm for pyruvate dehydrogenase complex (PDC) deficiency. Mol Genet Metab. 2017 Nov;122(3):61-66. doi:10.1016/j.ymgme.2017.09.001

Performance

Method Description

Pyruvate dehydrogenase complex (PDHC) enzyme is isolated using an immunocapture (enzyme-linked immunosorbent assay) method followed by colorimetric measurement of enzyme activity. Following addition of substrate to the isolated enzyme, PDHC activity is monitored colorimetrically and results are calculated based on the reduction of nicotinamide adenine dinucleotide (NAD[+]) to NADH.(Instruction manual: Pyruvate Dehydrogenase [PDH] Enzyme Activity Microplate Assay Kit. Abcam, Inc; 2012; Cowan T, Pasquali M: Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

PDF Report

No

Day(s) Performed

Varies

Report Available

60 to 70 days

Specimen Retention Time

6 months

Performing Laboratory Location

Rochester

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

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Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

84311-PDHC
88233-Fibroblast culture
88240-Cryopreservation for biochemical studies

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PDHC	Pyruvate Dehydrogenase Comp, Fibro	74577-8

Result ID	Test Result Name	Result LOINC® Value
30031	Interpretation (PDHC)	59462-2
30033	Reviewed By	18771-6
38064	PDHC	74577-8