



## Amino Acid Analysis

Test codes: 767X, 36183X, 29881X, 1776X, 19779X

### Clinical Use

- Diagnose primary aminoacidopathies
- Screen for secondary aminoacidopathies
- Monitor therapeutic response
- Assess nutritional status

### Clinical Background

Primary aminoacidopathies are typically autosomal recessive or X-linked inherited disorders resulting from a deficient enzyme or transport protein. Over 30 aminoacidopathies have been described in the literature. Symptoms range from relatively benign to severe and may include, but are not limited to, growth and mental retardation, developmental delay, learning disabilities, seizures, lethargy, coma, vomiting, metabolic acidosis or alkalosis, sudden infant death syndrome (SIDS), osteomalacia, and osteoporosis. Depending on the natural history of the disorder, symptoms may be minimized or prevented by early diagnosis and treatment. Treatment may be based on dietary restrictions and/or supplementation with cofactors (eg, riboflavin or cobalamin) or conjugating agents (eg, carnitine or sodium benzoate).

### Individuals Suitable for Testing

- Neonates/infants
- Children
- Adults

### Specimen Requirements

#### Plasma (full panel [767X], limited panel [1776X], or MSUD panel [19779X])

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

Alternatively, submit frozen plasma collected in EDTA (lavender-top tube) or lithium heparin (green-top tube). Separate plasma from cells as soon as possible.

Collect samples after an overnight (preferred) or 4-hour fast. Fasting not required for pediatric samples.

#### Urine (36183X)

2 mL frozen urine (random collection, no preservatives); 0.5 mL minimum

#### CSF (29881X)

1 mL frozen CSF (sterile screw cap container); 0.25 mL minimum

Plasma is preferred over urine except when abnormalities are more likely to manifest in urine (eg, disorders of transsulfuration, amino acid transport). CSF is used when suspecting disorders in which CSF levels are elevated relative to other sample types (eg, nonketotic hyperglycinemia).

### Method

- Liquid chromatography, mass spectrometry (LC/MS)
- Analytical sensitivity: 0.02-4.5  $\mu\text{mol/L}$ , depending on analyte
- Analytical specificity: no known cross-reaction with other substances
- Reportable range: 1.0-25,000  $\mu\text{mol/L}$
- CPT codes\*: 82139 (test codes 767X, 1776X, 29881X); 82136 (test code 19779X); 82139 and 82570 (test code 36183X)

### Reference Range

Reference ranges are provided in Tables 1-3 for plasma, urine, and CSF, respectively.

### Interpretive Information

Elevation of one or more amino acids may be diagnostic of an aminoacidopathy. Elevated amino acid levels are also associated with noninherited diseases such as severe liver disease and renal tubular disorders (eg, Fanconi syndrome). Decreased levels of amino acids are associated with malnutrition as seen in the elderly or those with poor protein intake or gastrointestinal disease.

Additional laboratory testing is required to diagnose other inherited disorders (ie, lactic acidosis, organic aciduria, and some urea cycle defects). Results should be evaluated in the context of clinical findings and/or additional test results.

Infant formulas that are supplemented with amino acids (particularly methionine and homocitrulline) and parenteral nutrition may affect the clinical accuracy of this test. Bacterial contamination of specimens and certain medications, such as valproic acid, can also affect the levels of specific amino acids. In addition, the absence of a protein-containing diet in newborns may preclude detection of selected aminoacidopathies.

Table 4 lists the amino acids that are elevated in the more common disorders.

Table 1. Plasma Amino Acid Age-Specific Reference Ranges (µmol/L)

Amino Acid	<1 month	1-23 months	2-17 years	Adults (≥18 years)
Aspartic acid	2-20	2-14	1-8	1-4
Glutamic acid	51-277	32-185	9-109	10-97
Hydroxyproline	13-72	7-63	6-32	4-27
Serine	87-241	83-212	85-185	65-138
Asparagine	12-70	20-77	23-70	31-64
α-Aminoadipic acid	≤3	≤4	≤2	≤2
Glycine	133-409	103-386	138-349	122-322
Glutamine	240-1194	303-1459	405-923	428-747
Sarcosine	≤5	≤4	≤4	≤4
β-Alanine	≤8	≤8	≤5	≤5
Taurine	29-161	26-130	32-114	31-102
Histidine	40-143	42-125	54-113	60-109
Citrulline	3-35	4-50	9-52	16-51
Arginine	14-135	30-147	38-122	43-407
Threonine	56-392	40-428	59-195	67-198
Alanine	83-447	119-523	157-481	200-483
1-Methylhistidine	≤4	≤9	≤27	≤47
γ-Aminobutyric acid	<1	<1	≤2	≤3
3-Methylhistidine	≤10	≤8	1-6	2-9
β-Aminoisobutyric acid	≤9	≤8	≤6	<1
Proline	87-375	104-348	99-351	104-383
Ethanolamine	8-106	5-19	5-15	5-13
α-Aminobutyric acid	1-20	4-30	6-30	7-32
Tyrosine <sup>a</sup>	33-160	24-125	31-108	38-96
Valine <sup>a,b</sup>	57-250	84-354	130-307	132-313
Methionine	13-45	12-50	14-37	16-34
Cystathionine	<1	<1	<1	<1
Isoleucine <sup>a,b</sup>	12-92	10-109	33-97	34-98
Leucine <sup>a,b</sup>	23-172	43-181	65-179	73-182
Homocystine	<1	<1	<1	<1
Phenylalanine <sup>a</sup>	30-79	31-92	38-86	40-74
Tryptophan <sup>a</sup>	17-85	16-92	30-94	40-91
Ornithine	29-168	19-139	33-103	27-83
Lysine	66-226	70-258	98-231	119-233
Alloisoleucine <sup>b</sup>	<1	<1	<1	<1

The full panel (767X) includes all amino acids listed except alloisoleucine.

<sup>a</sup>Included in the limited panel (1776X).

<sup>b</sup>Included in the MSUD panel (19779X).

Table 2. Urine Amino Acid Age-Specific Reference Ranges (mmol/mol creatinine)

Amino Acid	<1 month	1-23 months	2-17 years	Adults (≥18 yrs)
Aspartic acid	≤7.0	≤11.0	≤2.0	≤2.0
Glutamic acid	4-19	3-30	≤10.0	≤3.0
Hydroxyproline	30-485	2-345	≤4.0	≤2.0
Serine	44-454	39-422	13-127	10-71
Asparagine	8-42	5-132	3-42	2-37
α-Aminoadipic acid	≤10	≤36	≤34	≤11
Glycine	215-2053	105-413	23-413	≤330
Glutamine	≤355	41-396	18-188	21-182
Sarcosine	≤18	≤19	≤2	≤69
β-Alanine	≤9	≤15	≤5	≤10
Taurine	≤650	≤670	≤255	≤232
Histidine	40-301	56-543	9-425	17-266
Citrulline	≤4	≤13	≤4	≤2
Arginine	≤30	≤35	≤8	≤5

Table 2. Continued

Amino Acid	<1 month	1-23 months	2-17 years	Adults (≥18 yrs)
Threonine	≤112	9-158	4-60	4-46
Alanine	45-264	16-294	8-156	9-67
1-Methylhistidine	≤16	4-71	5-400	≤204
γ-Aminobutyric acid	≤1.4	≤1.5	≤1.6	≤1.6
3-Methylhistidine	9-45	14-35	11-40	10-35
β-Aminoisobutyric acid	≤269	≤309	≤133	≤88
Proline	≤219	≤216	≤11	≤2
Ethanolamine	87-490	54-176	27-114	21-65
α-Aminobutyric acid	≤7	≤7	≤5	≤2
Tyrosine	4-59	10-69	3-48	3-19
Valine	2-20	4-21	2-20	2-5
Methionine	≤7	≤7	≤5	≤2
Cystathionine	2-20	≤29	≤8	≤9
Isoleucine	≤9	≤12	≤5	≤3
Leucine	≤23	≤24	≤13	≤6
Homocystine	<1.0	≤4.0	<1.0	<1.0
Phenylalanine	3-24	6-39	2-22	2-9
Tryptophan	2-21	5-46	2-27	2-14
Ornithine	≤39	≤11	≤5	≤4
Lysine	13-284	4-239	3-112	3-59
Cystine	15-48	6-28	3-20	3-13
Hydroxylysine	5-117	2-72	≤8	≤8

Table 3. CSF Amino Acid Age-Specific Reference Ranges (μmol/L)

Amino Acid	<3 months	3-23 months	2-10 years	>10 years
Aspartic acid	≤2.7	<1.0	<1.0	≤2
Glutamic acid	1-9	≤5.1	≤10.6	1.1-13.2
Hydroxyproline	0.9-3.9	≤1.6	<1.0	≤1.7
Serine	30-88	22-61	15-62	9-41
Asparagine	≤27	≤13	≤25	≤24
α-Aminoadipic acid	<1.0	<1.0	<1.0	<1.0
Glycine	3-26	≤12	≤13	≤10
Glutamine	525-1583	386-742	377-1738	361-1175
Sarcosine	<1.0	<1.0	<1.0	<1.0
β-Alanine	<1.0	<1.0	<1.0	<1.0
Taurine	0-18	≤8	1-8	1-8
Histidine	8-32	4-25	7-25	7-22
Citrulline	1-4	≤3	1-2	≤2
Arginine	2-27	7-32	9-31	10-32
Threonine	23-104	10-55	8-85	12-64
Alanine	13-50	8-48	5-62	1-107
γ-Aminobutyric acid	<1.0	<1.0	≤2.2	≤3.1
β-Aminoisobutyric acid	<1.0	<1.0	<1.0	<1.0
Proline	≤3.9	≤2.3	≤1.7	≤5.9
α-Aminobutyric acid	≤6	≤6	1-11	1-11
Tyrosine	9-41	5-20	5-32	5-18
Valine	11-31	8-19	2-37	7-42
Methionine	2-14	1-7	≤9	1-8
Isoleucine	3-11	3-7	2-13	3-10
Leucine	7-22	7-12	8-27	9-32
Homocystine	<1.0	<1.0	≤2.5	≤2.1
Phenylalanine	4-31	4-14	≤25	6-31
Tryptophan	≤5.9	≤7.7	0.6-4.6	≤9.3
Ornithine	≤25.7	≤4.5	≤4.7	≤14.2
Lysine	6-38	3-29	9-58	19-60

Table 4. Common Aminoacidopathies and Associated Amino Acid Elevations

Common Aminoacidopathies	Elevated Amino Acids
<b>Primary Aminoacidopathies</b>	
Arginase deficiency	Arginine, glutamine
Arginosuccinase deficiency	Argininosuccinate, glutamine
Citrullinemia	Citrulline, glutamine
Cystinuria	Cystine, ornithine, lysine, arginine (urine only)
Homocystinuria	Homocystine
Maple Syrup Urine Disease (MSUD)	Valine, isoleucine, leucine, alloisoleucine
Phenylketonuria (PKU)	Phenylalanine
Tyrosinemia	Tyrosine
<b>Secondary Aminoacidopathies</b>	
Hyperammonemia	Glutamine
Lactic acidosis	Alanine
Organic acidurias, selected	Glycine
Transient tyrosinemia of the newborn	Tyrosine

## References

- Part 8. Amino Acids. In: Scriver CR, Beaudet AL, Valle D, Sly WS, Childs B, Kinzler KW, Vogelstein B, eds. *The Metabolic and Molecular Bases of Inherited Disease*. 8th ed. New York, NY: McGraw-Hill, Inc; 2001;1665-2105.
- Part IV. Disorders of amino acid metabolism and transport. Fernandes J, Saudubray J-M, Van den Berghe G, eds. *Inborn Metabolic Diseases: Diagnosis and Treatment*. 3rd ed. New York, NY: Springer; 2000;169-273.
- Part 2. Disorders of amino acid metabolism. Nyhan WL, Barshop BA, Ozand PT, eds. *Atlas of Metabolic Diseases*. 2nd ed. New York, NY: Oxford University Press Inc; 2005;109-189.
- Blau N, Duran M, Blaskovics ME, Gibson KM, eds. *Physician's Guide to the Laboratory Diagnosis of Metabolic Diseases*. 2nd ed. New York, NY: Springer; 2003.

\*The 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.

14225 Newbrook Drive  
PO Box 10841  
Chantilly, VA 20153-0841  
703-802-6900  
800-336-3718

33608 Ortega Highway  
San Juan Capistrano, CA 92690-6130  
949-728-4000  
800-642-4657  
www.nicholsinstitute.com

Quest, Quest Diagnostics, the associated logo, Nichols Institute and all associated Quest Diagnostics marks are the trademarks of Quest Diagnostics.  
© 2007 Quest Diagnostics Incorporated. All rights reserved.  
TS2202-HS 06/2007



Nichols Institute