

Inborn Errors of Amino Acid Metabolism

Many genetic errors affecting amino acid transport and metabolism have been identified. A defect of either function or catalytic activity results in the accumulation or excessive loss of 1 or more amino acids in biological fluids. Amino acids found in plasma, spinal fluid, and urine are the products of a complex system for transport and metabolism of the body's proteins and amino acids. Plasma free amino acid levels in healthy, well-nourished humans, 10 to 12 hours after a meal, show only slight day-to-day fluctuations and usually little variation from individual to individual unless there are large dietary differences. These steady-state concentrations represent a balance between utilization of amino acids by tissues and catabolism of the excess of proteins ingested as food or the body's own proteins. However, any interference or unusual event in the metabolism, growth, or replication of the body's cells and tissues that affects protein and amino acid metabolism will be accompanied, often dramatically, by changes in plasma and/or urinary amino acid levels. Thus, changes in amino acid profiles are sensitive indicators of a variety of physiological and pathological conditions.

Inborn errors of amino acid metabolism can manifest themselves at any time in a person's life, but most become evident in infancy and early childhood. Affected patients may have failure to thrive, neurological symptoms, digestive problems, locomotor retardation, and a wide spectrum of laboratory findings. If not diagnosed promptly and treated properly, these disorders can result in poor growth, mental retardation, and death. In situations where specific diet therapies are a part of the treatment regime, periodic amino acid analyses have to be scheduled to monitor the treatment progress. Other conditions where amino acid analysis may have clinical importance in the evaluation of several acquired conditions, including endocrine disorders, liver diseases, muscle diseases, neoplastic diseases, neurological disorders, nutritional disturbances, renal failure, and burns.

In our laboratory, quantitative and qualitative profiles of multiple or selected amino acids are determined using ion-exchange chromatography with ninhydrin detection, a high-pressure liquid chromatography (HPLC), and electrospray tandem mass spectrometry (MS/MS). When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing and in vitro confirmatory studies (enzyme assay, molecular analysis), name and phone number of key contacts who may provide these studies at Mayo or elsewhere, and a phone number to reach 1 of the laboratory directors in case the referring physician has additional questions.

References

Slocum RH, Cummings JG: Amino acid analysis of physiological samples. In Techniques in Diagnostic Human Biochemical Genetics. Edited by FA Hommes. New York, Wiley-Liss, 1995, pp 87-126

Amino acids, Part 8. In The Metabolic and Molecular Bases of Inherited Disease. 8th edition. Edited by CR Scriver, AL Beaudet, WS Sly, et al. New York, McGraw-Hill Book Company, 2001, pp 1667-2105

Amino Acid Reference Values

		Plasma Amino Acid Reference Values (Values Expressed as umol/L)				
		Age Groups				
		Premature	1-31 d	32 d-24 mo	25 mo-18 yr	> or = 19 yr
Phosphoserine	PSER	10-45	7-47	1-20	1-30	2-14
Taurine	TAU	151-411	46-492	15-143	10-170	54-210
Phosphoethanolamine	PETN	5-35	3-27	0-6	0-69	0-40
Aspartic Acid	ASP	24-50	20-129	0-23	1-24	1-25
Hydroxyproline	HYP	tr-80	0-91	0-63	3-45	0-53
Threonine	THR	150-330	90-329	24-174	35-226	60-225
Serine	SER	127-248	99-395	71-186	69-187	58-181
Asparagine	ASN	90-295	29-132	21-95	23-112	35-74
Glutamic Acid	GLU	107-276	62-620	10-133	5-150	10-131
Glutamine	GLN	248-850	376-709	246-1,182	254-823	205-756
Sarcosine	SAR	0	0-625	0	0-9	0
α -Aminoadipic Acid	AAD	0	0	0	0	0-6
Proline	PRO	92-310	110-417	52-298	59-369	97-329
Glycine	GLY	298-602	232-740	81-436	127-341	151-490
Alanine	ALA	212-504	131-710	143-439	152-547	177-583
Citrulline	CIT	20-87	10-45	3-35	1-46	12-55
α -Amino-n-butyric Acid	AANB	14-52	8-24	3-26	4-31	5-41
Valine	VAL	99-220	86-190	64-294	74-321	119-336
Cystine	CYS	15-70	17-98	16-84	5-45	5-82
Methionine	MET	37-91	10-60	9-42	7-47	10-42
Cystathionine	CYSTA	5-10	0-3	0-5	0-3	0-3
Isoleucine	ILE	23-85	26-91	31-86	22-107	30-108
Leucine	LEU	151-220	48-160	47-155	49-216	72-201
Tyrosine*	TYR	147-420	55-147	22-108	24-115	34-112
Phenylalanine*	PHE	98-213	38-137	31-75	26-91	35-85
β -Alanine	BALA	0	0-10	0-7	0-7	0-12
β -Aminoisobutyric Acid	BAIBA	0	0	0	0	0
Ethanolamine	ETN	na	0-115	0-4	0-7	0-153
Tryptophan	TRP	28-136	0-60	23-71	0-79	10-140
Hydroxylysine	HYL	0	0-7	0-7	0-2	0
Ornithine	ORN	77-212	48-211	22-103	10-163	48-195
Lysine	LYS	128-255	92-325	52-196	48-284	116-296
1-Methylhistidine	1-MHIS	4-28	0-43	0-44	0-42	72-124
Histidine	HIS	72-134	30-138	41-101	41-125	72-124
3-Methylhistidine	3-MHIS	5-33	0-5	0-5	0-5	0
Anserine	ANS	na	0	0	0	0
Carnosine	CARN	na	0-19	0	0	0
Arginine	ARG	34-96	6-140	12-133	10-140	15-128

na=control values not available

tr=trace

*Phenylalanine and tyrosine are available as separate tests.

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Spinal Fluid Amino Acid Reference Values
(Values Expressed as umol/L)

		Age Groups			
		1-31 d	32 d-23 mo	2-18 y	> or = 19 y
Taurine	TAU	10-51	5-18	4-16	4-15
Threonine	THR	40-189	17-73	13-55	3-53
Serine	SER	45-144	30-73	21-46	14-55
Asparagine	ASN	5-28	3-15	2-10	3-8
Glutamic Acid	GLU	0-17	0-8	0-6	0-8
Glutamine	GLN	542-1,493	374-848	376-806	375-1,010
Proline	PRO	1-10	0-7	0-19	0-3
Glycine	GLY	5-38	3-21	2-27	4-23
Alanine	ALA	20-70	17-74	14-53	18-62
Citrulline	CIT	1-6	0-6	0-6	0-2
α-Amino-n-butyric Acid	AANB	1-7	0-7	0-7	0-7
Valine	VAL	17-69	9-31	7-40	8-31
Cystine	CYS	0-6	0-7	0-3	0-3
Methionine	MET	3-23	2-13	2-6	1-9
Isoleucine	ILE	4-14	3-13	2-9	1-7
Leucine	LEU	8-36	6-22	6-20	6-16
Tyrosine	TYR	8-53	5-25	5-17	7-19
Phenylalanine	PHE	9-45	5-18	4-15	4-18
Ornithine	ORN	2-17	2-30	2-11	2-7
Lysine	LYS	15-51	10-57	12-38	17-32
Histidine	HIS	9-40	1-35	1-18	1-13
Arginine	ARG	4-27	13-35	10-28	11-25

Urine Amino Acid Reference Values
(24-Hour Values Expressed as umol/24 Hours)

		Age Groups	
		3-15 Years	> or =16 Years
Taurine	TAU	35-260	267-1,290
Threonine	THR	25-100	80-320
Serine	SER	93-210	200-695
Asparagine	ASN	15-40	34-100
Glutamic Acid	GLU	13-22	27-105
Glutamine	GLN	150-400	300-1,040
α-Aminoadipic Acid	AAD	25-78	0-165
Glycine	GLY	195-855	750-2,400
Alanine	ALA	65-190	160-690
Citrulline	CIT	0-13	0-11
α-Amino-n-butyric Acid	AANB	7-25	0-28
Valine	VAL	17-37	19-74
Cystine	CYS	11-53	28-115
Methionine	MET	7-20	5-30
Cystathionine	CYSTA	2-7	0-47
Isoleucine	ILE	3-15	4-23
Leucine	LEU	9-23	20-77
Tyrosine	TYR	30-83	38-145
Phenylalanine	PHE	20-61	36-90
β-Alanine	BALA	0-42	0-93
β-Aminoisobutyric Acid	BAIBA	25-96	10-235
Ornithine	ORN	3-16	5-70
Lysine	LYS	19-140	32-290
1-Methylhistidine	1-MHIS	41-300	68-855
Histidine	HIS	46-725	500-1,500
3-Methylhistidine	3-MHIS	42-135	64-320
Carnosine	CARN	34-220	16-125
Arginine	ARG	10-25	13-64

Urine Amino Acid Reference Values
(Random Values Expressed as nmol/mg Creatinine)

		Age Groups				
		Premature	1-31 d	32 d-24 mo	25 mo-18 yr	> or = 19 yr
Phosphoserine	PSER	500-1,690	150-339	112-304	70-138	40-510
Taurine	TAU	5,190-23,620	1,650-6,220	545-3,790	639-1,866	380-1,850
Phosphoethanolamine	PETN	80-340	0-155	108-533	18-150	20-100
Aspartic Acid	ASP	580-1,520	336-810	230-685	0-120	60-240
Hydroxyproline	HYP	560-5,640	40-440	0-4,010	0-3,300	0-26
Threonine	THR	840-5,700	445-1,122	252-1,528	121-389	130-370
Serine	SER	1,680-6,000	1,444-3,661	845-3,190	362-1,100	240-670
Asparagine	ASN	1,350-5,250	185-1,550	252-1,280	72-332	99-470
Glutamic Acid	GLU	380-3,760	70-1,058	54-590	0-176	39-330
Glutamine	GLN	520-1,700	393-1,042	670-1,562	369-1,014	190-510
Sarcosine	SAR	0	0-56	30-358	0-26	0-80
α -Aminoadipic Acid	AAD	70-460	0-180	45-268	2-88	40-110
Proline	PRO	1,350-10,460	370-2,323	254-2,195	0	0
Glycine	GLY	7,840-23,600	5,749-16,423	3,023-11,148	897-4,500	730-4,160
Alanine	ALA	1,320-4,040	982-3,055	767-6,090	231-915	240-670
Citrulline	CIT	240-1,320	27-181	22-180	10-99	8-50
α -Amino-n-butyric Acid	AANB	50-710	8-65	30-136	0-77	0-90
Valine	VAL	180-890	113-369	99-316	58-143	27-260
Cystine	CYS	480-1,690	212-668	68-710	25-125	43-210
Methionine	MET	500-1,230	342-880	174-1,090	16-114	38-210
Cystathionine	CYSTA	260-1,160	16-147	33-470	0-26	20-50
Isoleucine	ILE	250-640	125-390	38-342	10-126	16-180
Leucine	LEU	190-790	78-195	70-570	30-500	30-150
Tyrosine	TYR	1,090-6,780	220-1,650	333-1,550	122-517	90-290
Phenylalanine	PHE	920-2,280	91-457	175-1,340	61-314	51-250
β -Alanine	BALA	1,020-3,500	25-288	0-297	0-65	0-130
β -Aminoisobutyric Acid	BAIBA	50-470	421-3,133	802-4,160	291-1,482	10-510
Ethanolamine	ETN	na	840-3,400	0-2,230	0-530	0-520
Tryptophan	TRP	0	0	0-93	0-108	0-70
Hydroxylysine	HYL	na	10-125	10-97	40-102	40-90
Ornithine	ORN	260-3,350	118-554	55-364	31-91	20-80
Lysine	LYS	1,860-15,460	270-1,850	189-850	153-634	145-634
1-Methylhistidine	1-MHIS	170-880	96-499	106-1,275	170-1,688	170-1,680
Histidine	HIS	1,240-7,240	908-2,528	815-7,090	644-2,430	460-1,430
3-Methylhistidine	3-MHIS	420-1,340	189-680	147-391	182-365	160-520
Anserine	ANS	na	0-3	0-5	0	0
Carnosine	CARN	260-370	97-665	203-635	72-402	10-90
Arginine	ARG	190-820	35-214	38-165	31-109	10-90

na=control values not available

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Individual Amino Acid List

Alanine	Cystine	Ornithine
α -Aminoadipic Acid	Ethanolamine	Phenylalanine
α -Amino- <i>n</i> -Butyric Acid	Glutamic Acid	Phosphoethanolamine
Anserine	Glutamine	Phosphoserine
Arginine	Glycine	Proline
Argininosuccinic Acid	Histidine	Sarcosine
Asparagine	Hydroxylysine	Serine
Aspartic Acid	Isoleucine	Taurine
β -Alanine	Leucine	Threonine
β -Aminoisobutyric Acid	Lysine	Tryptophan
Carnosine	Methionine	Tyrosine
Citrulline	1-Methylhistidine	Valine
Cystathionine	3-Methylhistidine	