

CSF Amino Acids Reference Data and Interpretation

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Background

- CSF amino acid critical for diagnosis of GE and 3PD def, helpful for SO def
- Little published data
- Would not be able to sample healthy children

Data Review

- 5 year period
- 94 CSF samples received, investigation of infants with fits/seizures
- 17 excluded
 - evidence of blood staining
 - diagnosis of aa disorder
 - age >12 months

CSF amino acid concentrations

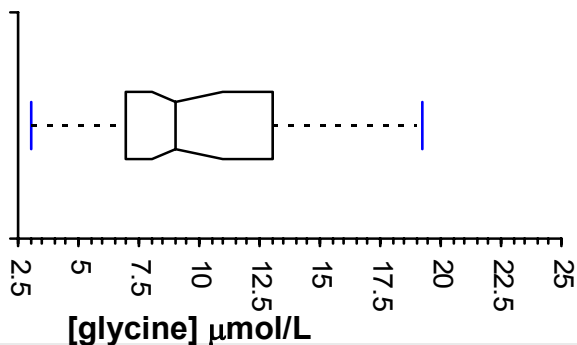
77 infants aged <12 months

Amino acid	Number of samples with detectable values	Range (umol/L)	Median umol/L	95 percentile (umol/L)
Taurine	77	5 – 65	21	6 - 62
Aspartate	77	3 – 27	6	3 – 17
Threonine	77	9 – 187	44	12 – 178
Serine	77	24 – 105	52	25 – 105
Asparagine	75	ND – 38	9	3 – 37
Glutamate	77	2 – 97	12	2 – 50
Glutamine	77	226 – 1014	449	231 – 940
Proline	1	ND – 8	ND	<1
Glycine	77	3 – 23	9	3 - 19
Alanine	77	12 – 62	33	15 – 60
Citrulline	38	ND – 9	3	0 – 9
Valine	77	5 – 49	19	7 – 48
Cystine	4	ND – 4	ND	<1
Methionine	66	ND – 36	6	2 – 30
Isoleucine	76	ND – 20	6	1 – 16
Leucine	77	5 – 38	15	5 – 35
Tyrosine	77	4 – 80	18	5 – 54
Phenylalanine	77	4 – 41	13	6 – 40
Ornithine	76	ND - 31	6	2 – 21
Lysine	77	6 – 51	20	7 – 42
Histidine	77	7 – 45	18	7 – 38
Tryptophan	0	ND	ND	<1
Arginine	72	ND - 41	19	7 – 40
s-sulphocysteine	0	ND	ND	<1

Data distributions for CSF glycine and serine concentrations (n=77)

Box; 25th – 75th percentiles, lines; 2.5th – 97.5th percentiles)

Glycine



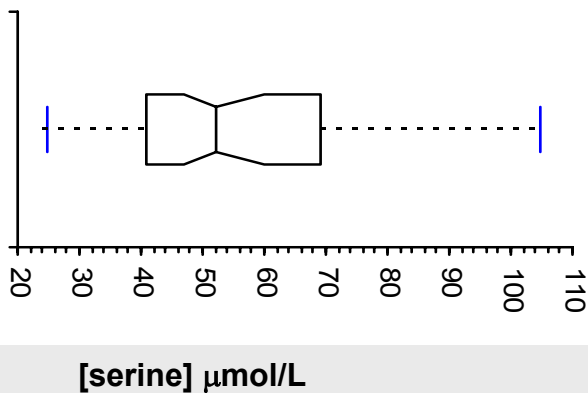
Median [glycine] = **9.0 μmol/L**

Range = **3-23 μmol/L**

2.5th percentile = **3.0 μmol/L**

97.5th percentile = **19.2 μmol/L**

Serine



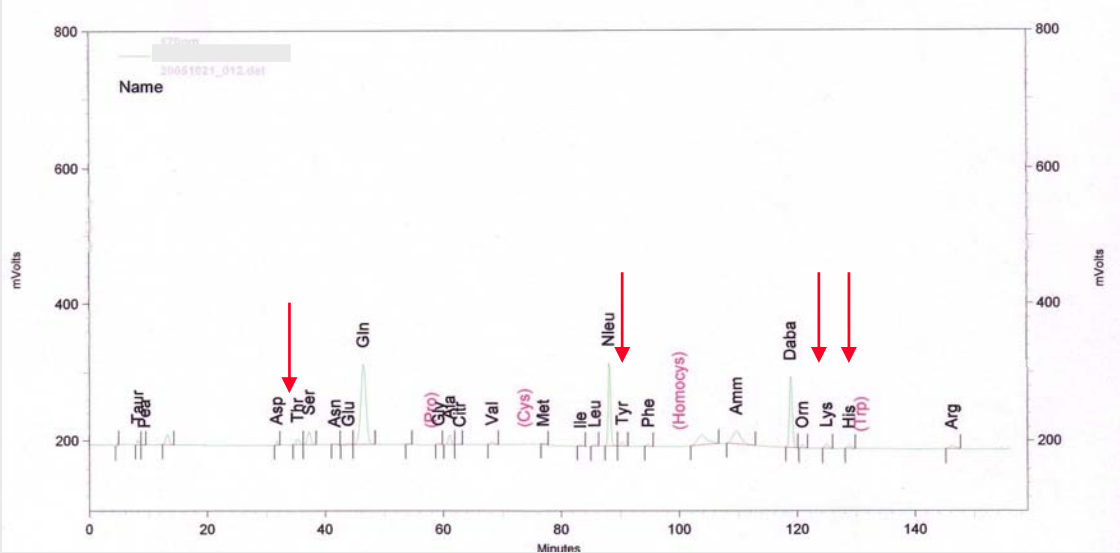
Median [serine] = **52.0 μmol/L**

Range = **24-105 μmol/L**

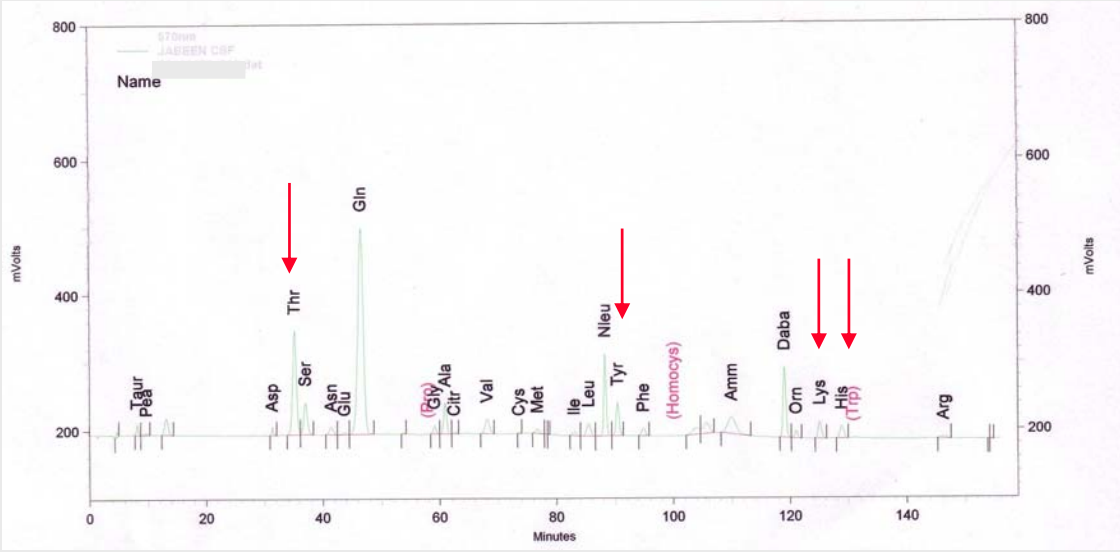
2.5th percentile = **25.0 μmol/L**

97.5th percentile = **105.0 μmol/L**

CSF Chromatograms

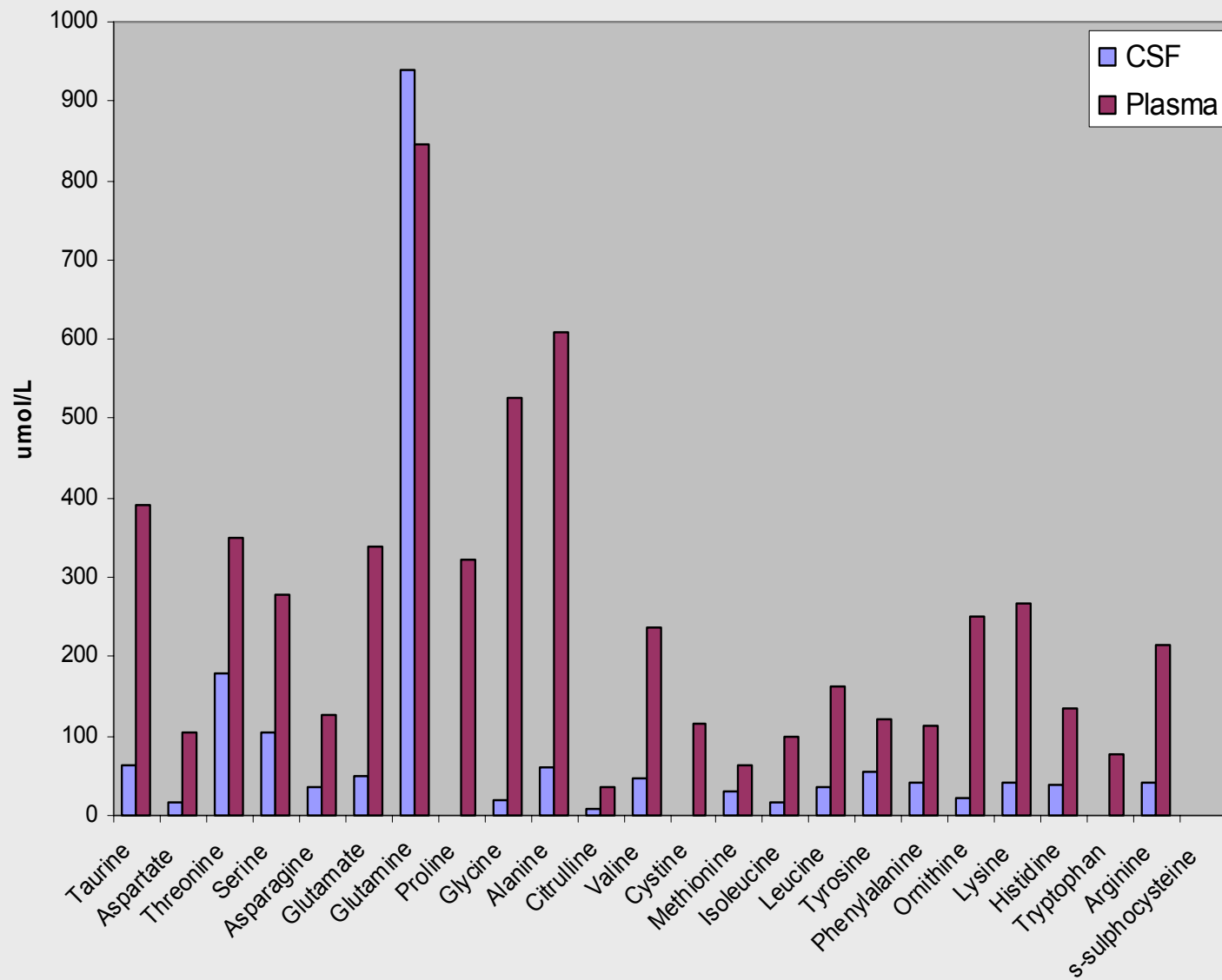


reference



Blood stained

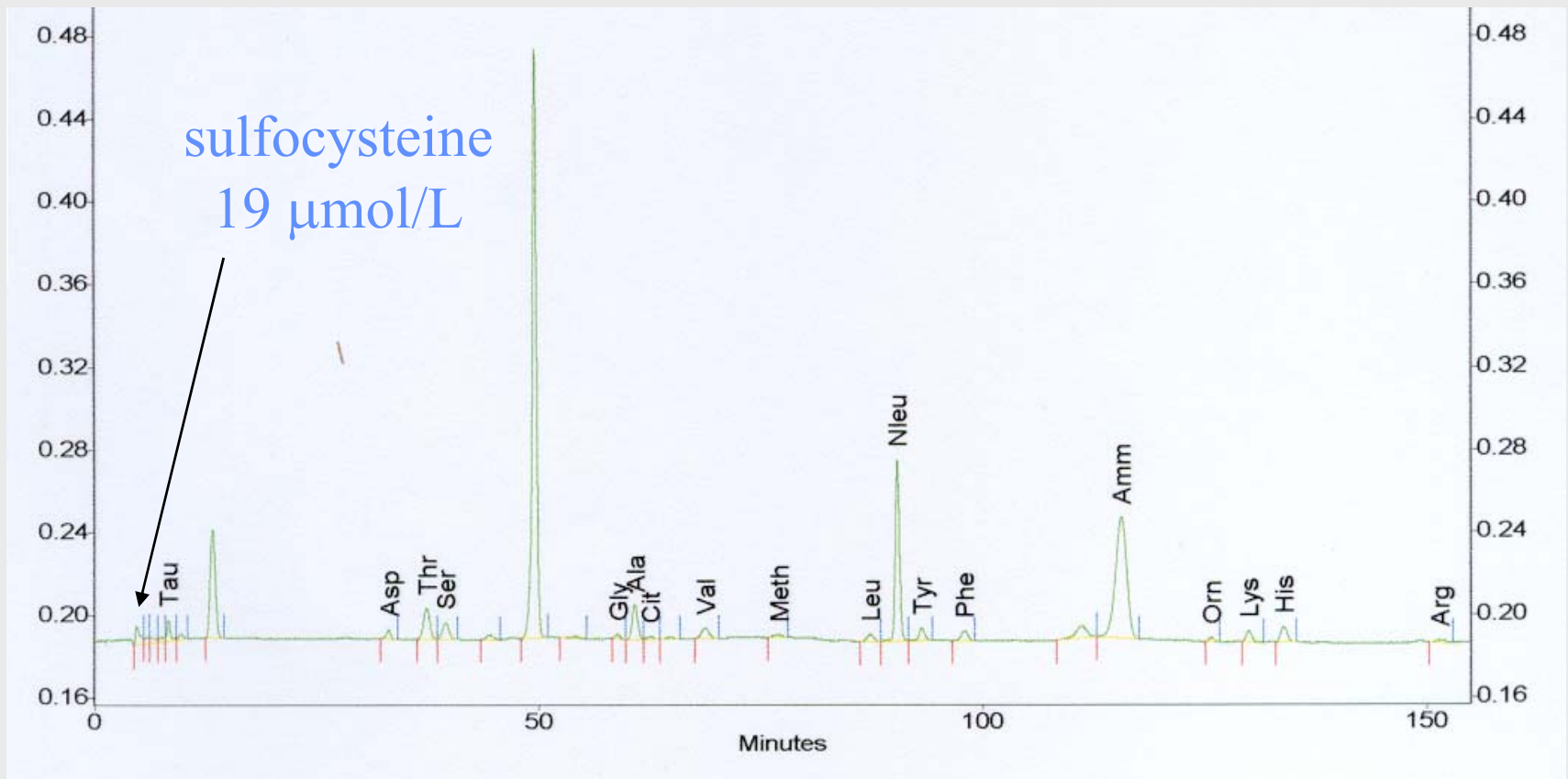
Amino acid concentrations; 95th Centile upper limits



Sulphite Oxidase Deficiency

- 3 cases in 5 years
- 1 isolated SO def
- 2 molybdenum cofactor def

CSF amino acids: Sulphite oxidase deficiency



Glycine and serine

- Glycine encephalopathy (NKH)
 - ↑ gly CSF, plasma, urine
 - Intractable seizures

- 3 phosphoserine dehydrogenase deficiency
 - ↓ ser CSF
 - Intractable seizures, microcephaly

Experience with GE

Case	CSF	plasma	ratio
Ref	3 - 19	220 - 527	< 0.08
1	241	904	0.27
2	206	1473	0.14
3	189	1401	0.13
4	134	610	0.22
5	104	227	0.46
6	135	732	0.18

Ante natal Rx 3PGD Deficiency

- Successful prenatal treatment of 3PGD def, De Koning et al Lancet Dec 2004 (364 p2221)
- 2 previous sibs
 - Serine suppl diet controlled seizures
 - Severe microcephaly
- Maternal serine supplementation *from 26 w*

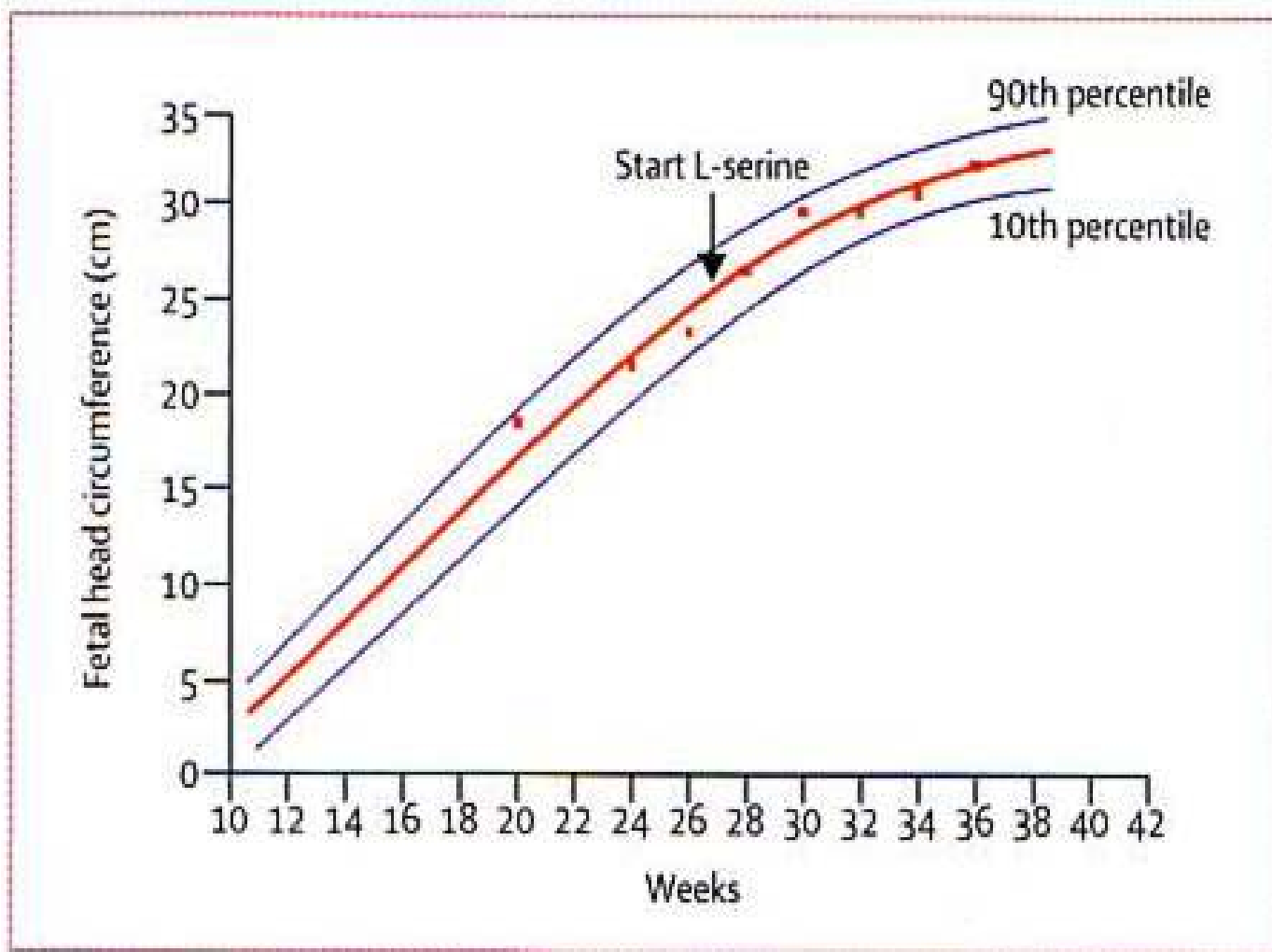


Figure: Fetal head circumference before and during maternal L-serine treatment

Prenatal serine therapy: outcome

- Healthy baby girl born at term
- Wt and ht on 40th centile, head 30th
- Cord plasma ser 52 umol/L (124 - 180)
- Serine supplements given from birth
- Child 4 yrs at time of report, growth neurological status and psychmotor dev normal