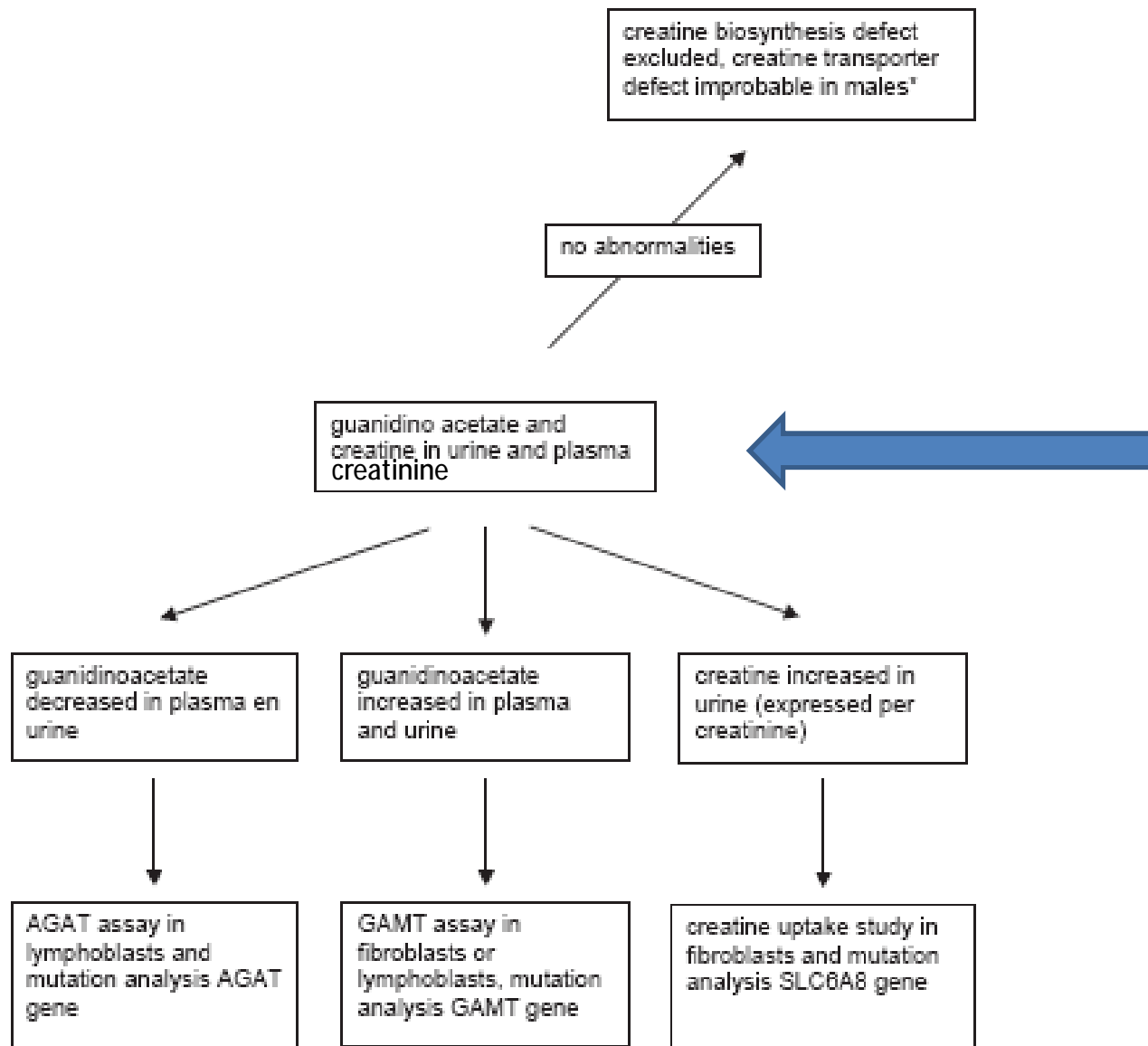


PERFORMANCE IN ERNDIM SPECIAL ASSAYS FOR CREATININE DISORDERS



Alberto Burlina & Cas Weykamp



ERNDIM Special Assay Schemes: Analytes 2007

Urine

5-OH-Indolacetic acid
Carnitine free
Creatine
Creatinine
Guanidinoacetate
Homovanillic acid
Hydroxyproline
Lactic acid
Mucopolysaccharides
Orotic acid
Pipelicolic acid
Sialic acid
Succinylacetone
Uric acid

Serum

3-OH Butyric acid
7-Dehydrocholesterol
Aceto acetate
C22:0 Behenic acid
C24:0 Lignoceric acid
C26:0 Cerotic acid
Carnitine free
Creatine
Guanidin acetic acid
Galactose
Homocysteine
Lactic acid
Phytanic acid
Pipelicolic acid
Pyruvic acid

Methods for the diagnosis of creatine deficiency syndromes:
A comparative study

Journal of Neuroscience Methods 156 (2006) 305–309

Table 1

Within-run and between-run imprecision results for GAA and Cr/Crn ratio as analysed by HPLC–MS/MS, GC–MS and HPLC methods

	GAA	Creatine
HPLC–MS/MS		
Within-run	5.2% (9.1)	1.5% (120.2)
Between-run	6.7% (9.9)	4.4% (120.7)
GC–MS		
Within-run	6.5% (24.4)	4.9% (35.2)
Between-run	6.9% (24.9)	4.5% (35.8)
HPLC		
Within-run 1	2.8% (72.8)	5.5% (2.534) ^a
Between-run	5.7% (357.0)	6.6% (9.333) ^a

S-Guanidinoacetate (17%)

Metods	N° Lab	%
GC/MS (with stable isotope dilution)	5	19,2
GC	1	3,8
LC-MS/MS	13	50,0
LC/MS	4	15,4
GC/MS	2	7,7
HPLC	1	3,8

S-Creatine (19%)

Metods	N° Lab	%
GC/MS (with stable isotope dilution)	5	17,2
GC	2	6,9
LC-MS/MS	13	44,8
LC/MS	4	13,8
GC/MS	2	6,9
HPLC	1	3,4
Other	2	6,9

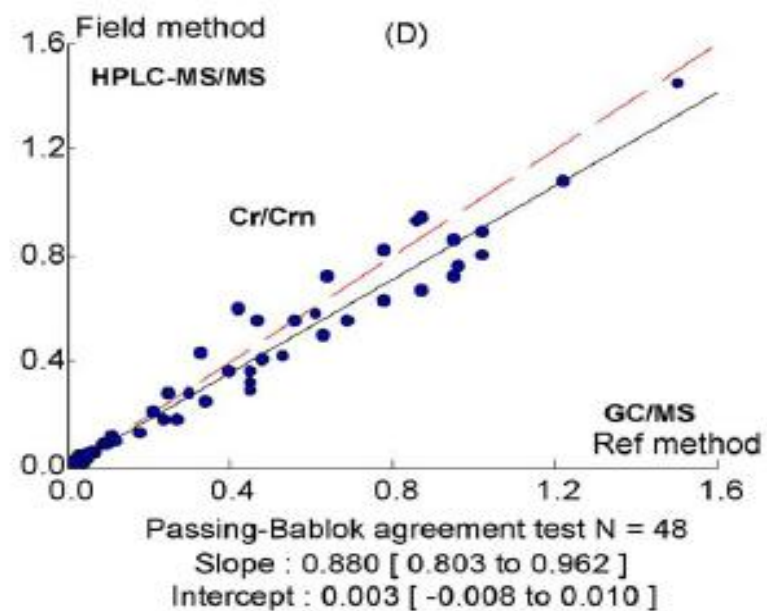
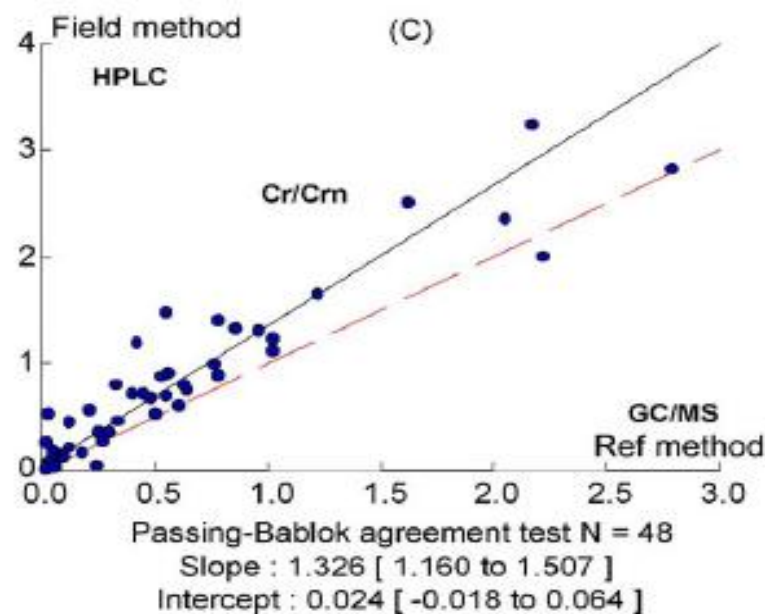


Table 2
Reference values for GAA (mmol/mol creatinine) and the Cr/Crn ratio in urine

	HPLC-MS/MS		HPLC		GC-MS	
	GAA (mmol/mol Crn)	Cr/Crn	GAA (mmol/mol Crn)	Cr/Crn	GAA (mmol/mol Crn)	Cr/Crn
Controls						
1 day-6 years (n=97)	73 ± 31 (13-139)	0.52 ± 0.39 (0.01-1.63)	76 ± 34 (13-124)	0.49 ± 0.37 (0.03-1.80)	75 ± 24 (11-131)	0.56 ± 0.42 (0.02-1.89)
7-16 years (n=37)	54 ± 19 (9-97)	0.26 ± 0.27 (0.02-1.10)	60 ± 18 (8-94)	0.44 ± 0.37 (0.03-1.44)	54 ± 16 (10-90)	0.25 ± 0.31 (0.02-1.22)
GAMT deficiency						
13 years (n=1)	380	0.80	386	0.89	356	0.71
CrT deficiency						
9-10 years (n=4)	58-70	2.2-3.1	48-69	2.8-4.2	62-67	2.9-3.0

Results are expressed as the average, standard deviation, and range. Values for one GAMT- and four CrT-deficient patients are also shown.

U-Creatinine (70%)

Metods	N° Lab	%
Jaffé end-point	24	26,7
Jaffé Kinetic	24	26,7
Hitachi	15	16,7
Dry Chemistry	15	16,7
HPLC	2	2,2
LC-MS/MS	3	3,3
Other	7	7,8

U-Creatine (24%)

Metods	N° Lab	%
GC/MS (with stable isotope dilution)	5	14,3
GC	1	2,85
LC-MS/MS	18	51,4
LC/MS	3	8,6
GC/MS	6	17,1
HPLC	2	5,7

U-Guanidinoacetate (26%)

Metods	N° Lab	%
GC/MS (with stable isotope dilution)	6	15,4
LC-MS/MS	18	46,2
GC/MS	8	20,5
HPLC	3	7,7
Other	4	10,3

Methodology and Quality Assurance in IEM Principles

Parameters for method validation
(details: ERNDIM web-site, <http://www.erndimqa.nl>)

• Specificity

• Selectivity

• Precision

→ Repeatability

→ Reproducibility

• Accuracy

• Recovery

• Range

• Linearity

→ Limit of detection

→ Limit of quantitation

Special assays serum 2007

	Creatine	Guanidinoacetate
Accuracy (Mean)	68,7	12,2
Precision (CV% Duplicates)	7,1%	8,4%
Linearity (r)	0,9834	0,9935
Recovery (%added analyte)	100%	112%
N° Lab.	33	30
Inter Lab CV	12%	15,2%

Special assays urine 2007

	Creatine	Creatinine	Guanidinoacetate
Accuracy (Mean)	329	7,77	116
Precision (CV% Duplicates)	8,8%	3,4%	6,1%
Linearity (r)	0,9927	0,9977	0,9865
Recovery (%added analyte)	116%	104%	107%
N° Lab.	43	100	46
Inter Lab CV	27%	5,7%	14,9%

PROPOSAL

Special Assays

a. Remove of hydroxyproline

b. Low level mevalonate

c. Low levels carnitine

d. Low levels 3-hydroxybutyrate, urate and creatine