Sentre name
Contact person

Address

Country

Participant: ..
Survey: 2/14
Samples sent: 10.03.2014
Case distributed: 15.09.2014

Bergen, 19.12.2014

Report: Porphyria External Quality Assessment Scheme 2/14

In this EQAS distribution, the quality control material came from a patient who had been predictively tested and shown to be genetically predisposed for acute intermittent porphyria (AIP). The material was sent to 37 laboratories, out of which 35 responded.

Please find in the following pages a detailed report including comparisons of the results from your laboratory with results from the other participants. Explanations of the graphs and figures are given on page 3. Details on factors of conversion, limits of acceptable deviation (quality specifications), laboratory report scoring and description of the method groups are found in the appendix.

Materials

The sample set consisted of 6 mL urine, 3 g faeces, 2 mL plasma, 1 mL EDTA whole blood and 2 x 500 µL pellets of red blood cells. The samples were sent frozen on dry-ice in March to all but one respondent. Twenty-tree of the centres receiving samples in spring stored them at -70°C or colder and 9 centres at -18°C to -20°C. Two centres did not report the storage temperature.

Results

Diagnostic strategies (n = 34)

The clinical information given with the samples was: *Male born 01.01.78, no symptoms, but a cousin with porphyria.*
Based on this, 26 laboratories would have chosen a first-line diagnostic strategy that as a minimum included plasma fluorescence scanning and urinary PBG and porphyrins. Twenty out of these would have included faecal porphyrin analysis (total or fractionation) and 14 also erythrocyte protoporphyrin (total or fractionation). Only one laboratory did not include plasma fluorescence scanning in their first-line diagnostic strategy. Thirteen laboratories would at some point in the diagnostic process have performed both PBG-deaminase and *HMBS* analysis, four only PBG-deaminase and one only *HMBS* in this case.

Thirteen laboratories reported that they decide what analyses are to be performed, three that the requesting physician alone decides and 16 that both decide.

Analytical performance

As in previous distributions, also with such low concentrations, substantial variations in analytical results are seen. All laboratories reported normal results for all porphyrin and porphyrin precursors when normalised by the upper reference limits, except for two borderline results for u-ALA and one increased result for plasma total porphyrins. In addition, one laboratory reported a positive plasma fluorescence

peak with maximum emission wavelength at 620 nm. Median PBG-deaminase activity when reported as percentage of the middle value of the reference range was 50% (n = 22). All but one laboratory out of the 17 reporting reference limits achieved a PBG-deaminase result below their lower reference limit, with median for normalised results at 0.71. The mutation c.346C>T was identified by all ten centres who performed sequencing of the *HMBS* gene in this patient.

Diagnosis, clinical interpretation and reporting

The samples in this case were from an asymptomatic and biochemically latent AIP patient with normal concentration levels of porphyrins and porphyrin precursors in all specimen types. In line with this, 33 out of 35 laboratories commented that there was no biochemical evidence to indicate any type of active porphyria in this patient, with the remaining two reporting a diagnosis of AIP without further comments on disease activity.

In total 12 laboratories reported a definitive diagnosis of (biochemically latent) AIP for this case. Nine confirmed their diagnosis by finding a mutation in the *HMBS* gene, and three by the finding of low PBG-deaminase activity alone. The latter three did not comment on the potential pitfalls of such an approach or suggested further follow-up analysis. Nine laboratories reported that the patient may be genetically predisposed to AIP/latent AIP and suggested further follow-up to confirm this diagnosis. Twelve laboratories reported that there was no sign of active porphyria disease in this patient. Ten of these included in their comments that latent porphyria had not been excluded and requested further information and/or samples from an affected family member. One laboratory reported that there were no abnormal biochemical results despite finding a positive plasma fluorescence peak and commented that they could not rule out asymptomatic familial PCT, requesting further samples. One laboratory reported potential interference in their HPLC methods and did not submit any diagnosis, but asked for new samples.

As is shown by the comments listed above, there is general consensus about reporting that the patient does not have active disease, but different strategies are in use as to how to handle that the patient belongs to a family with porphyria, when no further details are given. Some centres perform enzyme and DNA analysis directly, whereas others request details on family history and samples from the affected relative first. This is probably in reflection of local practise and varying availability of resources. For those laboratories that do not perform further testing it is, however, of importance that the requesting physician is informed that normal concentration levels of porphyrin precursors and porphyrins do not exclude latent porphyria and that strategies for further follow-up are suggested. We would also generally recommend that a definitive diagnosis of latent AIP is not established solely on a low PBG-deaminase activity result in patients with normal concentration levels of porphyrin precursors.

We are happy to receive any comments on this feedback report, as well as suggestions for improvement of the scheme. Please send your comments to porfyri@helse-bergen.no.

Kind regards,

Sverre Sandberg
General manager
on behalf of EPNET

Jørild H. Villanger

Aasne K. Aarsand

Interpretation of graphs and figures

General

- Values reported as “less than” (e.g. <5) are included in calculations as the value divided by 2.
- Results reported as “none detected” (nd), “undetectable” or “traces” are as a rule included in calculations as zero.
- Results reported as “-“ is interpreted as result not available and are not included in calculations.
- For the fractionations, the sum of uroporphyrin I/III, coproporphyrin I/III and total dicarboxylated porphyrins are calculated if not reported.
- Results excluded from the calculations (e.g. outliers, fractions not summing up to 100%, qualitative results) are given in brackets.
- Total porphyrins given in grams are converted to moles via the percentages of each porphyrin. If the percentages are not given, average factors of conversion are used.
- Results of faecal porphyrins given per gram are assumed to be per gram dry weight.
- Erythrocyte protoporphyrin results given per litre are assumed to be per litre erythrocytes (RBC).
- Reference intervals given in other units than the results are converted to the same units as the given results.

Statistical calculations

Number of reported results included (n) and excluded (n_X) from the calculations are given. For the main analytes the following are calculated for each method group; median, mean, standard deviation (SD), coefficient of variation (CV%) and number of results within method-related quality limits (n_{QL}). SD and CV% are not given for the method groups if less than 5 centres are included. For the fractionations the range is also reported, with all statistics being based on the results from HPLC based methods only.
Deviation is calculated as the difference between your result and the median in your method group. If the number of laboratories in a method group is <5 or the method used is characterised as “other”, the deviations are calculated compared to the overall median for all methods (starting from survey 1/10). The interval for acceptable deviation is calculated using method group median value ± deviation limit (see appendix).

How to read the reports

Histogram and numerical overview table
The histograms show the results of this survey (x-axis: concentration, in the unit given in the heading; y-axis: number of centres). Your result is given in a dark shade of green, with the exact value given in the legend. The other results in your method group are given in a lighter shade of green and the results for all the method groups in a pale shade of green. The orange bar along the x-axis gives the interval for acceptable deviation. The interval is not shown in the plot if neither result nor method group is reported. The statistics of this survey’s results are given in the table “Numerical overview”.

Historical data
The historical data section includes the results of the present as well as previous distributions. In the plot “Deviation (%)”, your results are chronologically plotted as percentage deviation from the method group median, with the most recent results at the top. In the plot "Deviation (concentration)”, your result is plotted as deviation from the method group median (in units of concentration) along the y-axis against the method group median on the x-axis. In both plots the grey shaded area mark acceptable deviation. Your current result is marked by ◆ and your previous results by ●. An arrow indicates results outside the scales of the plot.

Fractionations
In these tables the centre’s results and the statistics of this distribution’s results are presented. No historical data is given.

Qualitative PBG
The results for the qualitative PGB tests are presented as the number of positive and negative results for each method.

Enzyme activity
The enzyme activity results are presented as % of normal activity (% of the middle of the reference range). For centres that did not report this percentage, the reported result divided by the mean value of the corresponding reference range was included.

Plasma scan
The results are given as number of negative, inconclusive and positive/weak positive results in each method group. For positive/weak positive results the number of centres reporting emission peaks within and outside the expected area is reported.

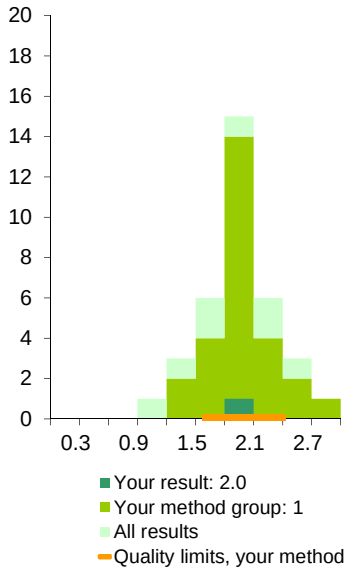
Normalised results
The reported results are divided by the corresponding upper reference limits and presented as a ratio. No historical data is given.

Selected analyses
The table shows your choice together with the number of centres selecting the analytes as first-line, second-line, third-line or later, and the number not selecting the analytes. If you have only scored some of the fractions, the scoring of ≥ 2 fractions will be scored as selected fractionation.

Laboratory report score
The laboratory reports were judged by criteria developed on the basis of the Best Practice Guidelines of the Swiss Society of Medical Genetics, see appendix for details.

u-ALA [µmol/mmol creatinine] reported by 35 out of 35 laboratories

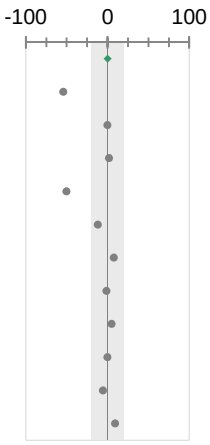
Histogram



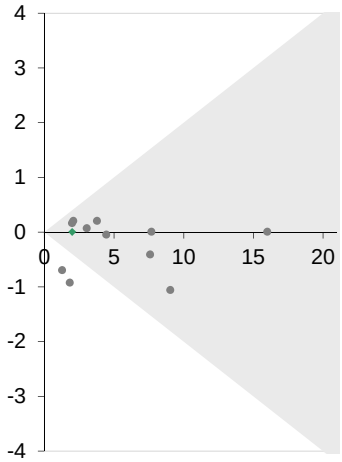
Historical data:

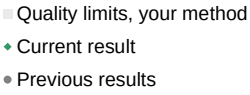
Survey	Median	Your result	Dev.%
2/14	2.0	2.0	0.0
1/14	1.3	0.6	-53.8
2/13	16.0	16.0	0.0
1/13	3.1	3.1	2.1
2/12	1.9	0.9	-50.0
1/12	9.1	8.0	-11.7
2/11	2.0	2.2	7.8
1/11	4.5	4.4	-1.1
2/10	3.8	4.0	5.3
1/10	7.7	7.7	0.0
2/09	7.6	7.2	-5.4
1/09	2.1	2.3	9.5

Deviation (%)



Deviation (concentration)





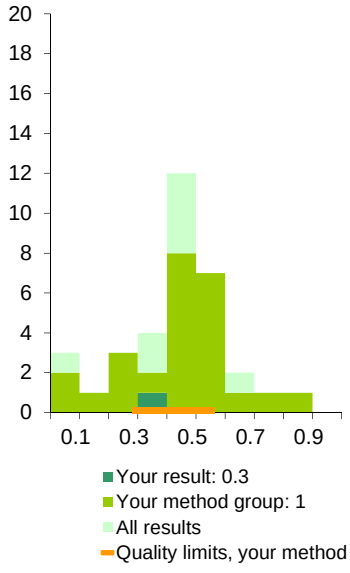
Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 Bio-Rad Column Test	27	0	2.0	2.0	0.3	16.1	22	
2 Ion exchange + Ehrlich reaction	7	0	2.1	2.0	0.4	21.3	4	
3 HPLC	1	0	1.0	1.0			0	
0 Other	0	0	–	–			0	
All centres	35	0	2.0	1.9	0.4	18.9	26	

n: results included, n_X: results excluded from calculations, n_{QL}: results within method-related quality limits.

u-PBG [µmol/mmol creatinine] reported by 35 out of 35 laboratories

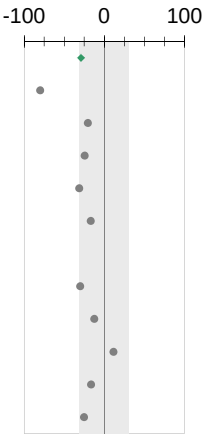
Histogram



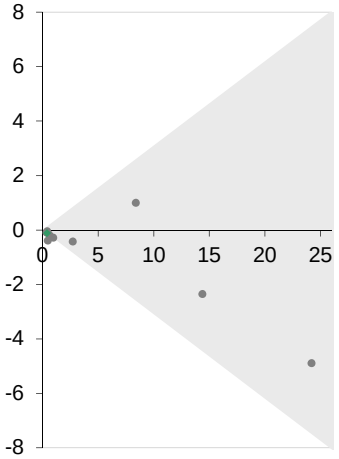
Historical data:

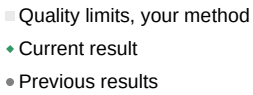
Survey	Median	Your result	Dev.%
2/14	0.4	0.3	-28.9
1/14	0.5	0.1	-79.9
2/13	24.2	19.3	-20.2
1/13	0.5	0.4	-24.0
2/12	0.7	0.5	-30.9
1/12	14.4	12.0	-16.4
2/11	0.5	NC	NC
1/11	1.0	0.7	-29.6
2/10	0.5	0.4	-12.1
1/10	8.4	9.4	11.8
2/09	2.7	2.3	-16.1
1/09	0.4	0.3	-25.0

Deviation (%)



Deviation (concentration)





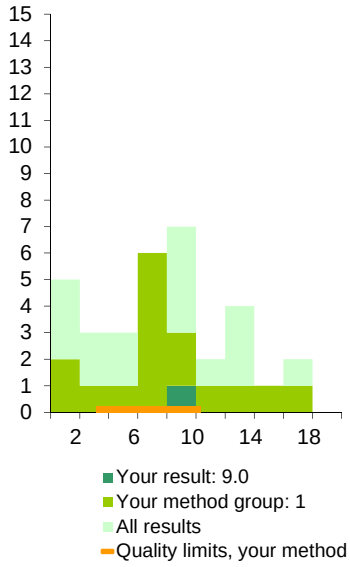
Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 Bio-Rad Column Test	26	1	0.4	0.4	0.2	44.2	17	
2 Ion exchange + Ehrlich reaction	7	0	0.4	0.4	0.1	23.1	6	
3 HPLC	1	0	0.1	0.1			0	
0 Other	0	0	–	–			0	
All centres	34	1	0.4	0.4	0.2	43.3	23	

n: results included, n_X: results excluded from calculations, n_{QL}: results within method-related quality limits.

Total u-porphyrins [nmol/mmol creatinine] reported by 34 out of 35 laboratories

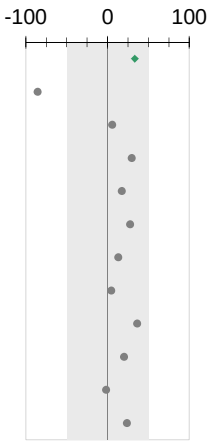
Histogram



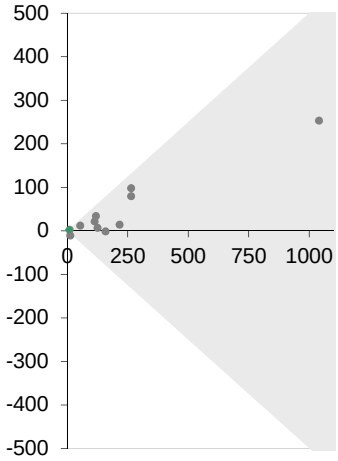
Historical data:

Survey	Median	Your result	Dev.%
2/14	6.8	9.0	33.3
1/14	13.7	2.0	-85.4
2/13	217	230	6.2
1/13	265	344	29.8
2/12	114	134	17.9
1/12	120	153	27.8
2/11	10.6	12.0	13.4
1/11	126	132	4.9
2/10	265	362	36.6
1/10	54.9	66.2	20.6
2/09	159	157	-1.3
1/09	1041	1293	24.2

Deviation (%)



Deviation (concentration)



Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 HPLC as sum of fractions	17	1	6.8	7.8	4.3	55.5	10	
2 Extraction + spectroscopy	5	0	9.5	8.1	5.7	70.2	2	
3 Acidification + spectroscopy	11	0	8.0	7.4	4.9	65.8	5	
0 Other	0	0	–	–			0	
All centres	33	1	7.8	7.7	4.6	59.3	17	

n: results included, n_X: results excluded from calculations, n_{QL}: results within method-related quality limits.

u-porphyrin fractions [%] reported by 32 out of 35 laboratories *

Porphyrin	n	n_X	Your result	Median	Range	Mean	SD	Comments
Uro total	29	2	11	10	0 - 32	11	7.1	
Uro I	16	2	NA	6	0 - 14	6	3.7	
Uro III	16	2	NA	2	0 - 7	3	2.3	
Hepta	29	2	4	3	0 - 9	3	2.2	
Hexa	28	2	0	0	0 - 3	1	1.0	
Penta	28	2	0	1	0 - 7	2	2.1	
Copro total	29	2	85	84	57-100	84	9.1	
Copro I	26	2	21	21	14 - 34	22	4.9	
Copro III	26	2	64	63	43 - 77	63	7.2	

* The statistical calculations include only the results in method group 1 (HPLC; n=31).

Qualitative PBG reported by 18 out of 35 laboratories

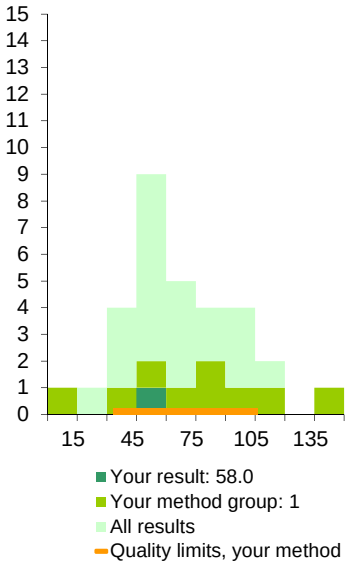
Your result is marked by yellow

Method	TT	HT	WS	O	Sum	Comments
Negative	6	6	6	0	18	
Positive	0	0	0	0	0	
Positive (+)	0	0	0	0	0	
Positive (++)	0	0	0	0	0	
Positive (+++)	0	0	0	0	0	

Methods: TT: Ion-Exchange + colourimetric (Thermo Trace PBG test kit)
HT: Hoesch test
WS: Watson-Schwartz test (modified or unmodified)
O: Other

Total f-porphyrins [nmol/g dry wt] reported by 31 out of 35 laboratories

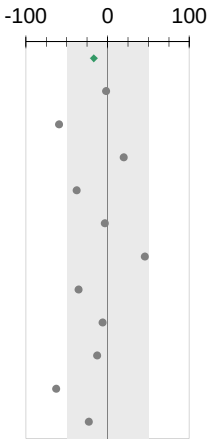
Histogram



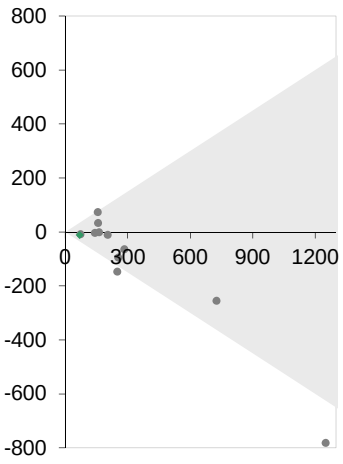
Historical data:

Survey	Median	Your result	Dev.%
2/14	69.6	58.0	-16.7
1/14	163	161	-1.3
2/13	252	103	-59.0
1/13	160	192	20.3
2/12	256	160	-37.5
1/12	144	140	-2.8
2/11	158	231	46.0
1/11	728	472	-35.2
2/10	206	194	-5.6
1/10	75.2	66.0	-12.2
2/09	1252	470	-62.5
1/09	285	220	-22.7

Deviation (%)



Deviation (concentration)



Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 HPLC as sum of fractions	10	0	69.6	73.5	36.6	49.8	7	
2 Extraction + spectroscopy	21	0	59.0	63.5	22.7	35.8	16	
0 Other	0	0	–	–			0	
All centres	31	0	60.0	66.7	27.7	41.6	23	

n: results included, n_X: results excluded from calculations, n_{QL}: results within method-related quality limits.

f-porphyrin fractions reported by 30 out of 35 laboratories *

Porphyrin	n	n_X	Your result	Median	Range	Mean	SD	Comments
Uro total (%)	22	5	0	0	0 - 8	1	2.0	
Uro I (%)	16	5	NA	1	0 - 3	1	1.1	
Uro III (%)	16	5	NA	0	0 - 4	1	1.2	
Hepta (%)	22	5	0	0	0 - 3	0	0.7	
Hexa (%)	21	5	0	0	0 - 1	0	0.3	
Penta (%)	21	5	0	0	0 - 1	0	0.3	
Copro total (%)	25	5	31	29	5 - 69	30	17.1	
Copro III:I ratio	*28*	*1*	*0.4*	*0.5*	*0.2 - 0.7*	*0.5*	*0.1*	
Isocopro (%)	17	5	NA	0	0 - 1	0	0.4	
Dicarboxylated total (%)	25	5	69	70	23 - 95	68	18.4	
Proto (%)	23	5	69	56	13 - 90	51	22.6	
Other dicarboxylated (%)	19	6	NA	17	0 - 48	22	16.6	

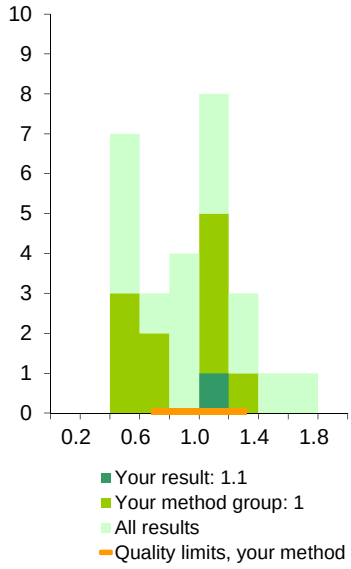
* The statistical calculations are based on full fractionation results in method group 1 (HPLC; n=30).

Faeces dry weight [%] reported by 24 out of 35 laboratories

Porphyrin	n	n_X	Your result	Median	Range	Mean	SD	Comments
Percentage dry weight	23	1	32	34	31 - 40	35	2.5	

Total e-protoporphyrin [µmol/L erythrocytes] reported by 27 out of 35 laboratories

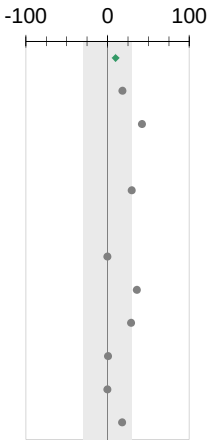
Histogram



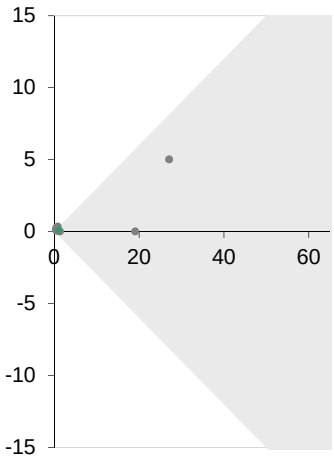
Historical data:

Survey	Median	Your result	Dev.%
2/14	1.0	1.1	10.0
1/14	27.1	32.1	18.5
2/13	0.6	0.8	42.4
1/13	1.1	NG	NG
2/12	0.5	0.6	30.0
1/12	0.7	NP	NP
2/11	19.1	19.1	0.0
1/11	0.9	1.2	36.4
2/10	0.5	0.7	29.2
1/10	0.9	0.9	1.0
2/09	1.4	1.4	0.0
1/09	0.5	0.6	18.2

Deviation (%)



Deviation (concentration)



Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 HPLC as sum of fractions	11	0	1.0	0.8	0.3	35.1	7	
2 Fluorescence spectroscopy (incl. Hematofluorimeter)	15	0	0.9	0.9	0.4	38.9	7	
0 Other	1	0	0.5	0.5			0	
All centres	27	0	0.9	0.9	0.3	38.1	14	

n: results included, n_X: results excluded from calculations, n_{QL}: results within method-related quality limits.

Zinc/Free protoporphyrin [%] reported by 26 out of 35 laboratories *

Porphyrin	n	n_X	Your result	Median	Range	Mean	SD	Comments
Zinc protoporphyrin	25	1	91	82	33-100	78	15.3	
Metal-free protoporphyrin	25	1	9	19	0 - 67	23	15.2	

* The statistical calculations include results from method group 1 (HPLC as sum of fractions; n=10) and method group 2 (fluorescence spectroscopy incl. hematofluorimeter; n=16).

Enzyme activity [percent of middle reference range] reported by 22 out of 35 laboratories *

	n	n_X	Your result	Median	Range	Mean	SD	CV%	Comments
Porphobilinogen deaminase activity	22	0	20	48	20 - 84	50	13.7	27.3	
Uroporphyrinogen decarboxylase activity	9	0	NA	96	85 - 150	104	20.8	19.9	

* The statistical calculations include results from both method groups. For measurement of porphobilinogen deaminase activity 3 centres used HPLC (group 1) and 19 centres used fluorescence spectroscopy (group 2). For measurement of uroporphyrinogen decarboxylase activity 8 centres used HPLC (group 1), and one centre used fluorescence spectroscopy (group 2).

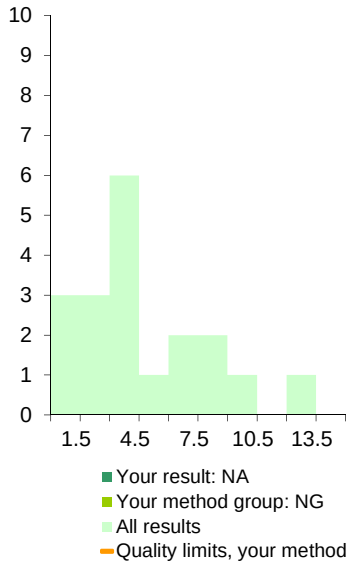
DNA analysis reported by 10 out of 35 laboratories

Ten centres identified the mutation c.346C>T by sequencing the HMBS gene. One of these additionally sequenced the UROD gene and did not identify any mutation.

You reported:

Total plasma porphyrins [nmol/L] reported by 19 out of 35 laboratories

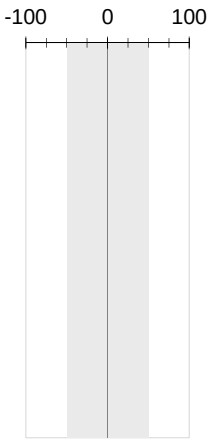
Histogram



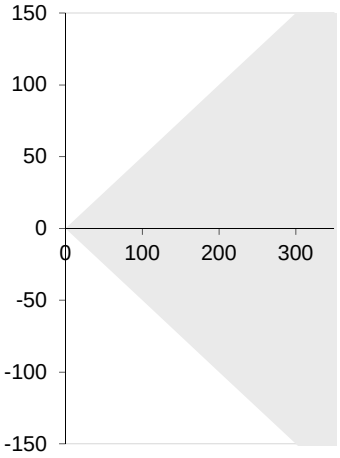
Historical data:

Survey	Median	Your result	Dev.%
2/14	–	NA	NA
1/14	–	NA	NA
2/13	–	NA	NA
1/13	–	NG	NG
2/12	–	NG	NG
1/12	–	NA	NA
2/11	–	NG	NG
1/11	–	NG	NG
2/10	–	NG	NG
1/10	–	NG	NG
2/09	–	NG	NG
1/09	–	NG	NG

Deviation (%)



Deviation (concentration)



Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 HPLC as sum of fractions	8	0	6.0	6.0	3.0	49.8	6	
2 Spectroscopy without HPLC	11	0	3.1	3.7	3.5	96.3	6	
0 Other	0	0	–	–			0	
All centres	19	0	4.2	4.7	3.4	73.9	12	

n: results included, n_X: results excluded from calculations, n_{QL}: results within method-related quality limits.

p-porphyrin fractions [%] reported by 9 out of 35 laboratories *

Porphyrin	n	n_X	Your result	Median	Range	Mean	SD	Comments
Uro total	9	0	NA	2	0 - 49	14	19.9	
Uro I	5	0	NA	0	0 - 21	6	9.2	
Uro III	5	0	NA	0	0 - 25	5	11.2	
Hepta	9	0	NA	0	0 - 4	1	1.4	
Hexa	9	0	NA	0	0 - 7	2	2.6	
Penta	9	0	NA	0	0 - 13	2	4.1	
Copro total	9	0	NA	51	0 - 100	55	37.9	
Copro I	7	0	NA	25	0 - 100	34	33.3	
Copro III	7	0	NA	20	0 - 52	19	18.6	
Proto	7	0	NA	49	0 -72	35	33.4	

* The statistical calculations include only the results in method group 1 (HPLC; n=9).

Plasma scan [number of centres] reported by 34 out of 35 laboratories

Method group	n	Negative results	Inconclusive results	Positive/weak positive results with emission peak			Comments
				≤ 623	> 623	NC / NG	
1 (with rs-PMT/CCD)	23	22	0	1	0	0	
2 (without rs-PMT)	6	6	0	0	0	0	
3 (unknown PMT)	5	5	0	0	0	0	
All centres	**34**	**33**	**0**	**1**	**0**	**0**	
Your result; method gr. 1		Neg					

Plasma ALA and PBG reported by 1 out of 35 laboratories

One center reported a result for ALA of 0.1 nmol/L and a result for PBG of 5.9 nmol/L.

You reported:

Normalised results (ratio between reported results and the corresponding upper reference limit)

	n	n_x	Your result	Median	Range	Mean	SD	CV%	Comments
u-ALA	34	0	0.4	0.5	0.3 - 1.1	0.6	0.2	39.7	
u-PBG	34	0	0.4	0.4	0.0 - 1.0	0.4	0.2	52.3	
Total u-porphyrin	26	1	0.3	0.3	0.0 - 0.7	0.3	0.2	59.2	
Total f-porphyrin	25	0	NR	0.4	0.2 - 0.7	0.4	0.2	41.0	
Total e-protoporphyrin	23	1	0.6	0.6	0.3 - 0.9	0.6	0.2	31.9	
Total p-porphyrin	17	0	NA	0.2	0.0 - 1.3	0.3	0.3	104	

Selected analyses in this case history reported by 34 out of 35 laboratories

Given the case history (see appendix) and the results of your analyses, we asked in which order you would have requested/performed the following analyses, according to your routine procedures.

	Your data [a]	No of centres scoring analysis as [a]			Not selected	Comments
		1	**2**	**3**		
u-ALA	1	25	4	1	4	
u-PBG (quantitative)	1	27	3	2	2	
u-PBG (qualitative)	–	12	0	0	22	
Total u-porphyrin	1	27	1	1	5	
u-porphyrin fractionation	2	8	15	2	9	
u-uroporphyrin isomers	–	7	6	2	19	
u-other analyses	–	0	0	1	33	
Total f-porphyrin	1	19	4	2	9	
f-porphyrin fractionation	1	8	10	4	12	
f-coproporphyrin isomers	–	6	8	3	17	
f-other analyses	–	0	0	1	33	
Total e-proto-porphyrin	1	14	6	1	13	
Zinc proto-porphyrin	1	7	12	2	13	
Metal-free protoporphyrin	1	9	10	2	13	
other whole blood	–	1	0	1	32	
p-fluorescence scan	1	32	1	0	1	
p-ALA/PBG	–	1	0	0	33	
Total p-porphyrin	–	2	8	2	22	
p-porphyrin fractionation	–	0	3	3	28	
p-other analyses	–	0	0	0	34	
Enzyme: PBG-deaminase[1]	3	9	6	2	17	
DNA: HMBS gene[2]	–	2	4	8	19	

[a] The numbers denote the following: 1 Analysis requested as first-line based on clinical information, 2 Second-line analysis based on the results from first-line analyses, 3 further analyses requested/performed in this case. "–" denotes 'Not selected'.

[1] Two centres selected uroporphyrinogen decarboxylase (score 3) instead. In addition to porphobilinogen deaminase two centres selected uroporphyrinogen decarboxylase (score 2) and one centre selected coproporphyrinogen oxidase and protoporphyrinogen oxidase (score 2).

[2] One centre selected UROD-gene analysis (score 3) instead. Three centres, in addition to HMBS-gene analysis, selected the UROD (score 2), PPOX (scores 1 and 2) and FECH (score 3) genes.

Laboratory report score

A laboratory report was submitted form 28 of the 35 centres. Nineteen of the reports included all the 15 criteria. Eight reports fulfilled from 12 to 14 criteria, whereas one report scored less than 10. Date of arrival/registered and interpretation of results given and advice on further testing if appropriate were the criteria most often lacking. Patient name, material tested, analyses performed, quantitative or qualitative results given, units stated and reference intervals specified were criteria included in all the reports. Reports written in languages we do not master may not be optimally scored, and if so, we apologise for this.

Your score:

Your attached laboratory report achieved 15 points.

Conclusion

You correctly reported that there was no biochemical evidence to indicate any type of active porphyria in this patient, and that the patient may be genetically predisposed to AIP (latent AIP), suggesting further follow-up to confirm this diagnosis.

Other comments

Appendix

Clinical case history 2/14

Male born 01.01.78, no symptoms, but a cousin with porphyria.

Sample data relevant for EQAS Survey 2/14

Urine creatinine 16.9 mmol/L Haematocrit 46 % Haemoglobin 15.8 g/dL Reticulocyte count 0.059 $x10^{12}$/L

Method groups 2/14

Please notify us if your methods have been categorised in the wrong method group.

Matrix	*Analyte*	*Method group*
Urine	ALA	1 Bio-Rad ALA/PBG by Column Test 2 Ion-Exchange + Ehrlich reaction (not Bio-Rad) 3 HPLC (with fluorescence, MS or other detection) 0 Other:
	PBG	1 Bio-Rad ALA/PBG by Column Test 2 Ion-Exchange + Ehrlich reaction (not Bio-Rad) 3 HPLC (with fluorescence, MS or other detection) 0 Other:
	Total porphyrins	1 HPLC as sum of fractions (with fluorescence, MS or other detection) 2 Extraction (liquid-liquid or solid phase) + spectroscopy, including BioRad porphyrins by column test 3 Acidification + spectroscopy (fluorescence or UV/VIS) 0 Other:
	Porphyrin fractions	1 HPLC (with fluorescence, MS or other detection) 0 Other: Spectrofluorometric method; Cromatographic-spectrophotometric method
Faeces	Total porphyrins	1 HPLC as sum of fractions (with fluorescence, MS or other detection) 2 Extraction (with or without SPE) + spectroscopy (fluorescence or UV/VIS) 0 Other:
	Porphyrin fractions	1 HPLC (with fluorescence, MS or other detection) 0 Other:
Whole blood	Total proto-porphyrins	1 HPLC as sum of fractions (with fluorescence, MS or other detection) 2 Fluorescence spectroscopy (incl. Hematofluorimeter) with or without extraction 0 Other: Spectrophotometry
	Zinc/free proto-porphyrins	1 HPLC (with fluorescence, MS or other detection) 2 Fluorescence spectroscopy (incl. Hematofluorimeter) with or without extraction 0 Other: Qualitative fluorescence spectroscopy
Pellet of RBC	Enzyme activity (PBGD, UROD)	1 HPLC (with fluorescence, MS or other detection) 2 Fluorescence spectroscopy (no HPLC) 0 Other:
Plasma	ALA/PBG	1 HPLC (with fluorescence, MS or other detection) 2 Solid phase extraction (SPE) (C8, C18, ion-exchange, etc.) + fluorescence spectroscopy 0 Other: Colorimetric assay
	Total porphyrins	1 HPLC as sum of fractions (with fluorescence, MS or other detection) 2 Spectroscopy (Fluorescence or UV/VIS) without HPLC 0 Other:
	Porphyrin fractions	1 HPLC (with fluorescence, MS or other detection) 0 Other: Fluorescence spectroscopy
	Plasma scan	1 Fluorescence spectroscopy with red sensitive photomultiplier or charge-coupled device 2 Fluorescence spectroscopy without red sensitive photomultiplier 3 Fluorescence spectroscopy, unknown photomultiplier 0 Other:

Recommended units

For porphyrin precursors in urine:	µmol/mmol creatinine
For porphyrins in urine:	nmol/mmol creatinine
For porphyrins in faeces:	nmol/g dry weight
For protoporphyrin in erythrocytes:	µmol/L erythrocytes

Appendix continued

Analytical quality specifications

Analytic quality specifications for urinary ALA, PBG and total porphyrins have been established using data on biological variation from patients with stable acute porphyria (Aarsand AK et al, Clin Chem 2006). "Desirable" analytical quality is calculated as total allowable error (TE_a): $0.25*\sqrt{(CV_I^2+CV_G^2)} + 1.65*(0.5\ CV_I)$, where CV_I is the within-subject/intra-individual and CV_G the between-subject biological variation (Petersen PH et al, Ann Clin Biochem 2002). Since biological variation data are not available for plasma and fecal total porphyrins and erythrocyte protoporphyrin, data on urinary markers were used as basis to set TE_a for these parameters. The quality specifications used are given for each analyte in the table below.

Limits of acceptable deviation from method median; desirable analytical quality

Urinary ALA	±20 %
Urinary PBG	±31 %
Urinary total porphyrins	±50 %
Faecal total porphyrins	±50 %
Erythrocyte total protoporphyrin	±30 %
Plasma total porphyrins	±50 %

Scoring of laboratory reports

The laboratory reports were judged by criteria developed on the basis of the Best Practice Guidelines of the Swiss Society of Medical Genetics (http://www.sgmg.ch/user_files/images/SGMG_Reporting_Guidelines.pdf, accessed December 2009). The following 15 criteria were awarded one point if fulfilled/present; laboratory name, laboratory contact details (address/telephone/fax), date of report, name of referring doctor/report destination, patient name, patient date of birth (or ID number), date of sampling, date of arrival/registered, material tested, analyses performed, quantitative or qualitative results given, units stated, reference intervals specified, interpretation of results given and advice on further testing if appropriate, and name/signature of verifying/responsible laboratory personnel.

Abbreviations in use

NA	analysis not available at the laboratory	SD	standard deviation
NP	analysis not performed (but available)	CV%	coefficient of variation (%) (= SD x 100 divided by the mean)
NG	result not given	n	number of reported results included in the calculations
NC	result not possible to include in calculations	n_X	number of reported results excluded from the calculations
NR	no reference limit given	n_{QL}	number of reported results within method-related quality limits

Factors of conversion

Results given in grams were transformed to moles using the factors given in the table below. Total porphyrin values were calculated by converting each porphyrin from grams to moles and then added up to a total value.

Component	***Molcular weight [g/mol]***	***Factor of conversion*** (multiply by factor to convert)		
			from	to
Creatinine	113.12	8.840	g	mmol
ALA	131.13	7.626	mg	µmol
PBG	226.23	4.420	mg	µmol
Uroporphyrin I/III	830.76	1.204	µg	nmol
Heptacarboxylporphyrin I	786.75	1.271	µg	nmol
Hexacarboxylporphyrin I	742.74	1.346	µg	nmol
Pentacarboxylporphyrin I	698.73	1.431	µg	nmol
Coproporphyrin I/III	654.72	1.527	µg	nmol
Protoporphyrin IX	562.66	1.777	µg	nmol
Zinc protoporphyrin	626.03	1.597	µg	nmol
Isocoproporphyrin	654.71	1.527	µg	nmol
Other dicarboxylated (comprises other di-/tricarboxylated than protoporphyrin such as pempto-, deutero-, meso-, harderoporphyrins)		1.862	µg	nmol
If only total porphyrins are reported, then the following average factors of conversion are used:				
Total u-porphyrins		1.356	µg	nmol
Total f-porphyrins		1.540	µg	nmol
Total e-protoporphyrin		1.687	µg	nmol
Total p-porphyrins		1.652	µg	nmol