Sentre name
Contact person

Address

Country

Participant: …
Survey: 2/18
Samples sent: 12.03.2018
Case distributed: 10.09.2018

Bergen, 21.12.2018

Report: Porphyria External Quality Assessment Scheme 2/18

Thank you for submitting results for the Porphyria External Quality Assessment Scheme survey 2/18. 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 (analytical performance specifications), laboratory report scoring and description of the method groups are found in the appendix (page 11-12).

Materials and respondents

This autumn there were two set of samples. This is the report for the first set 2/18:
Samples came from a male born 1944 with bullae and fragile skin consistent with porphyria and the request to provide recommendations for treatment and follow-up. The sample set consisted of 6 mL urine, 4 g faeces, 2.5 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 this spring to 37 laboratories, and with gel packs to two laboratories in August. Seven laboratories reported storing the samples frozen at minus 20°C and 22 at minus 70°C or colder. In total 38 laboratories submitted results for the 2/18 case, eight of these were received after the deadline.

Results

Diagnosis: PCT

Diagnostic strategies

All 38 laboratories would have performed either quantitation or fractionation of urinary porphyrins at some point during the diagnostic process, with urinary porphyrins (quantitation or fractionation) being selected as first-line by 32 of the laboratories. Plasma fluorescence scanning was selected as first-line by 30 laboratories and as second-line by four. Analysis of faecal porphyrins (quantitation or fractionation) was selected as first-line by 17 laboratories and as second-line by 17. Three laboratories would not have fractionated urinary porphyrins, four laboratories would not have performed plasma fluorescence scanning, and three laboratories would not have analysed faecal total porphyrins or fractions at any point in the diagnostic process. Twenty-two laboratories would have performed either analysis of the UROD enzyme (n = 5), the UROD gene (n = 7) or both (n = 10).

Analytical performance

All but one laboratory reported increased urinary total porphyrin results, but with a very large dispersion, ranging from 6.3 - 1365 nmol/mmol creatinine, with a median result of 677 nmol/mmol creatinine. When results were normalised to the upper reference limit, the median was 23 (range 0.2 - 78.7, n = 33). The between-laboratory CV was 44 %, i.e. in the same range as the last survey including a patient with

symptomatic PCT (1/16). No obvious differences between methods was observed in the present survey. All but one laboratory found that porphyrins in urine mostly consisted of uro- and heptaporphyrins, with median levels 70 % and 20 %, respectively (n = 31, after exclusion of 4 outliers). The median urinary uro-heptaporphyrin ratio was 3.6 (1.2 - 4.5, n = 31). All 33 centres performing plasma fluorescence scanning reported a positive result, 32 with wavelengths ranging from 616 - 620 nm, and one at 632 nm. Twenty-four laboratories submitted results for isocoproporphyrin in faeces, with a median percentage at 12 % (range 0 -34 %). Seven laboratories reported normal UROD activity and two reduced activity (n = 9). Nine participants performed UROD sequencing, all reporting a negative result.

Diagnosis, clinical interpretation and reporting

The samples came from a patient with PCT, and 36 out of 38 participants reported this diagnosis. Consensus is that this patient has sporadic PCT, as was reported by twelve laboratories based on results of UROD activity and/or UROD sequencing. Two reported likely familial PCT after finding reduced UROD enzyme activity. Most participants based their PCT diagnosis on increased concentrations of uro- and heptaporphyrins in urine, the plasma fluorescence emission wavelength and the presence of isocoproporphyrin in faeces/a normal faecal coproporphyrin III:I ratio. Two laboratories reported incorrect diagnoses; one EPP and one CEP, both likely caused by incorrect analytical results and interpretation.

As part of the provided clinical information, advice on treatment and follow-up was requested. Twenty-five centres provided this, in the form of detailed information on treatment and follow-up, or a reference to a website where this information could be found. Eight centres recommended referral to a specialist/ specialist centre.

The centres providing information on treatment and follow-up offered advice on how to identify and manage predisposing factors, recommendations on skin protection and avoidance of sun and treatment options phlebotomies, chloroquine and for one centre, also iron chelators. However, the level of detail varied between participants, and there were some variations in the recommendations given. There is a need for the development of common guidelines, as will be initiated by EPNET in the coming years. This will help facilitate harmonised best practise treatment and follow-up.

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 Jørild H. Villanger Aasne K. Aarsand
General manager on behalf of EPNET

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 “-“ are 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 performance specifications (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. 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 PBG tests are presented as the number of positive and negative results for each method.

Enzyme activity

The enzyme activity results are presented as % of lower value of the reference range.

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

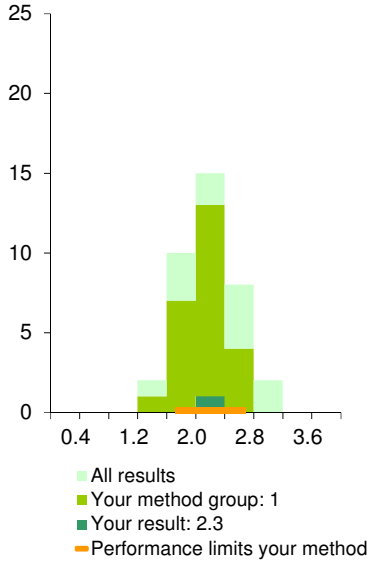
The table shows your choice together with the number of centres selecting the analytes as first-line, second-line or third-line, and the number not selecting the analytes.

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 37 out of 38 laboratories

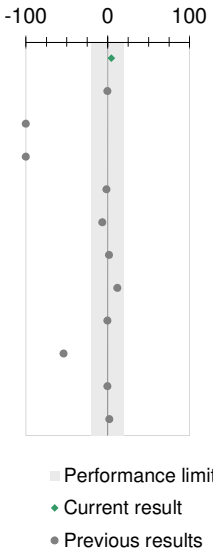
Histogram



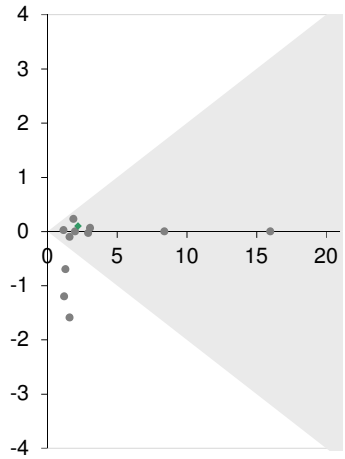
Historical data:

Survey	Median	Your result	Dev.%
2/18	2.2	2.3	4.5
1/18	8.4	8.4	0.0
2/17	1.6	0.0	-100
1/17	1.2	0.0	-100
2/16	2.9	2.9	-1.1
1/16	1.6	1.5	-6.3
2/15	1.2	1.2	2.1
1/15	1.9	2.1	12.3
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

Deviation (%)



Deviation (concentration)



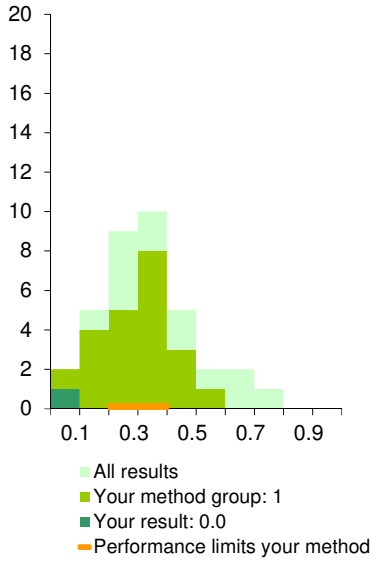
Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 Bio-Rad Column Test	25	0	2.2	2.1	0.3	14.8	21	
2 Ion exchange + Ehrlich reaction	11	0	2.4	2.3	0.5	21.9	7	
3 HPLC	1	0	1.6	1.6			0	
0 Other	0	0	–	–			0	
All centres	37	0	2.2	2.2	0.4	17.8	28	

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

u-PBG [µmol/mmol creatinine] reported by 37 out of 38 laboratories

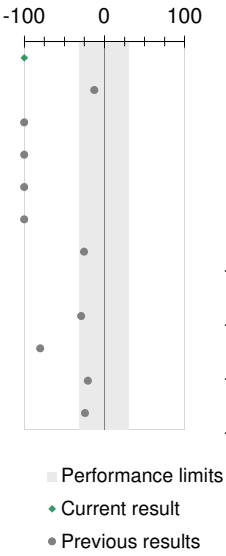
Histogram



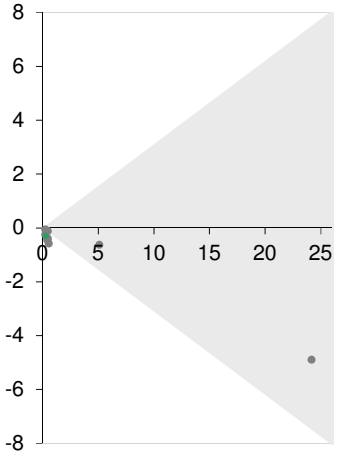
Historical data:

Survey	Median	Your result	Dev.%
2/18	0.3	0.0	-100
1/18	5.1	4.5	-12.3
2/17	0.6	0.0	-100
1/17	0.5	0.0	-100
2/16	0.4	0.0	-100
1/16	0.3	0.0	-100
2/15	0.3	0.2	-25.3
1/15	0.3	NC	NC
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

Deviation (%)



Deviation (concentration)



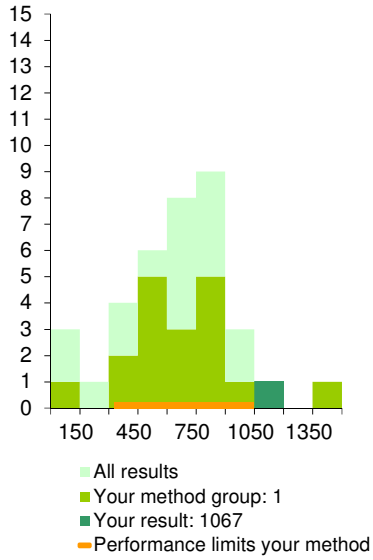
Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 Bio-Rad Column Test	23	1	0.3	0.3	0.1	50.9	11	
2 Ion exchange + Ehrlich reaction	12	0	0.4	0.4	0.2	40.3	7	
3 HPLC	1	0	0.1	0.1			0	
0 Other	0	0	–	–			0	
All centres	36	1	0.3	0.3	0.2	53.4	18	

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

Total u-porphyrins [nmol/mmol creatinine] reported by 36 out of 38 laboratories

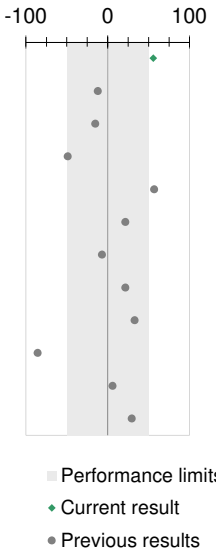
Histogram



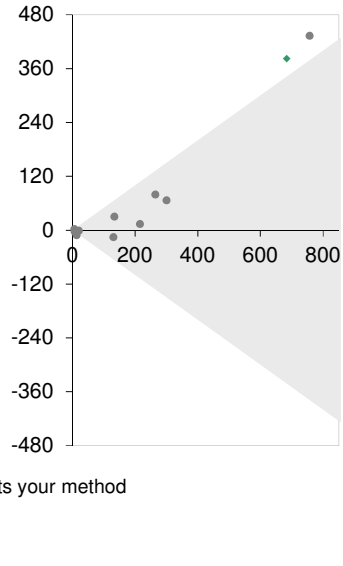
Historical data:

Survey	Median	Your result	Dev.%
2/18	685	1067	55.9
1/18	132	116	-11.9
2/17	11.8	10.0	-14.9
1/17	7.8	4.0	-48.6
2/16	758	1191	57.1
1/16	134	164	22.0
2/15	21.4	20.0	-6.5
1/15	301	367	21.9
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

Deviation (%)



Deviation (concentration)



Numerical overview

Method group	n	n_X	Median	Mean	SD	CV%	n_{QL}	Comments
1 HPLC as sum of fractions	19	0	685	685	283	41.4	16	
2 Extraction + spectroscopy	5	0	662	515	305	59.2	4	
3 Acidification + spectroscopy	12	0	719	634	288	45.5	10	
0 Other	0	0	–	–			0	
All centres	36	0	677	644	285	44.3	30	

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

u-porphyrin fractions [%] reported by 36 out of 38 laboratories *

Porphyrin	n	n_X	**Your result**	Median	Range	Mean	SD	Comments
Uro total	31	5	**76**	70	46 - 93	69	8.1	
Uro I	19	5	**NA**	55	41 - 75	56	8.5	
Uro III	18	5	**NA**	16	0 - 23	15	6.2	
Hepta	31	4	**17**	20	17 - 32	21	3.5	
Hexa	30	4	**0**	1	0 - 4	1	1.1	
Penta	30	4	**4**	5	0 - 13	6	2.8	
Copro total	32	4	**3**	4	2 - 12	5	2.1	
Copro I	27	4	**1**	1	1 - 4	2	0.8	
Copro III	27	4	**2**	3	2 - 5	3	0.9	

* The statistical calculations include only the results in method group 1 (HPLC; n=36).

Qualitative PBG reported by 15 out of 38 laboratories * Your result is marked by yellow

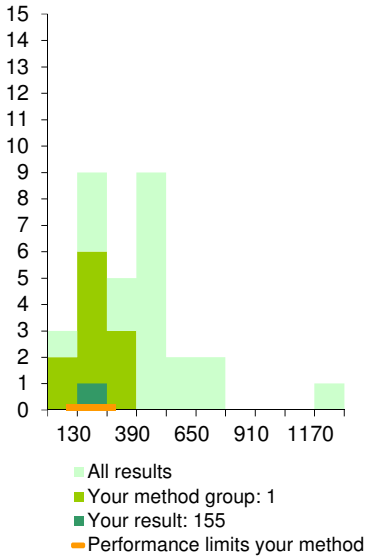
Method	IE	HT	WS	O	Sum	Comments
Negative	2	8	4	0	15	
Positive	0	0	0	0	0	
Positive (+)	0	0	0	0	0	
Positive (++)	0	0	0	0	0	
Positive (+++)	0	0	0	0	0	

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

* One centre reported a negative result without reporting the method.

Total f-porphyrins [nmol/g dry wt] reported by 32 out of 38 laboratories

Histogram

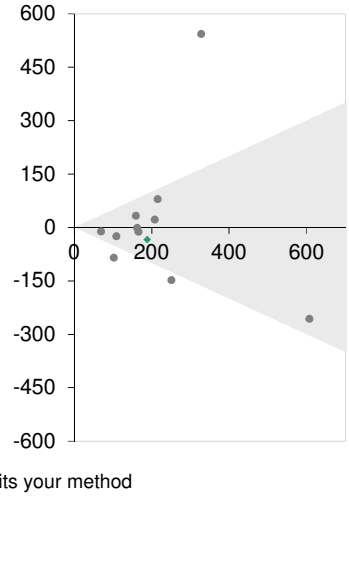


Historical data:

Survey	Median	Your result	Dev.%
2/18	189	155	-18.0
1/18	608	351	-42.3
2/17	103	17.0	-83.5
1/17	209	230	10.3
2/16	328	871	165
1/16	166	153	-7.8
2/15	216	295	36.5
1/15	109	84.0	-23.0
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

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	189	208	79.6	38.2	9	
2 Extraction + spectroscopy	20	1	458	447	246	55.0	14	
0 Other	0	0	–	–			0	
All centres	31	1	350	363	232	64.1	23	

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

f-porphyrin fractions reported by 31 out of 38 laboratories *

Porphyrin	n	n_X	**Your result**	Median	Range	Mean	SD	Comments
Uro total (%)	27	2	**12**	5	0 - 13	5	3.8	
Uro I (%)	18	2	**NA**	3	0 - 6	3	2.0	
Uro III (%)	18	2	**NA**	1	0 - 3	1	1.0	
Hepta (%)	27	2	**43**	23	0 - 47	22	11.0	
Hexa (%)	26	2	**3**	6	0 - 13	6	3.8	
Penta (%)	26	2	**11**	7	0 - 24	9	5.4	
Copro total (%)	28	2	**15**	13	5 - 41	15	8.3	
Copro III:I ratio	*30*	*1*	***0.4***	*0.4*	*0.3 - 1.5*	*0.6*	*0.3*	
Isocopro (%)	22	3	**NA**	12	0 - 34	13	7.2	
Di-/tricarboxylated total (%)	28	2	**14**	32	7 - 66	34	15.6	
Proto (%)	25	3	**14**	7	3 - 60	11	13.3	
Other di-/tricarboxylated(%)	21	3	**NA**	26	0 - 42	25	12.0	

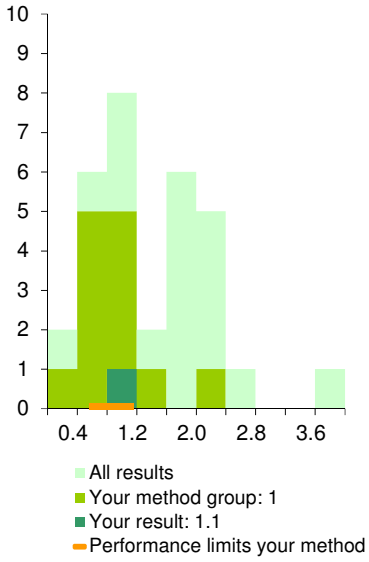
* The statistical calculations are based on full fractionation results in method group 1 (HPLC; n=31). One of the centres only reported the coproporphyrin isomer ratio.

Faeces dry weight [%] reported by 28 out of 38 laboratories

Porphyrin	n	n_X	**Your result**	Median	Range	Mean	SD	Comments
Percentage dry weight	28	0	**30**	32	26 - 40	32	3.0	

Total e-protoporphyrin [µmol/L erythrocytes] reported by 31 out of 38 laboratories

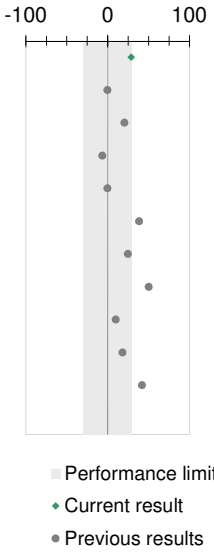
Histogram



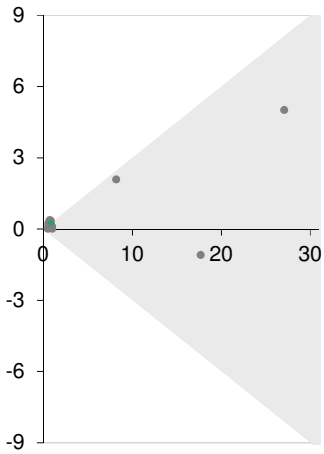
Historical data:

Survey	Median	Your result	Dev.%
2/18	0.9	1.1	29.0
1/18	1.0	1.0	0.0
2/17	0.6	0.7	20.7
1/17	17.7	16.6	-6.2
2/16	0.5	0.5	0.0
1/16	0.9	1.2	38.7
2/15	8.2	10.3	25.2
1/15	0.7	1.1	50.7
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

Deviation (%)



Deviation (concentration)



Numerical overview

Method group	n	n_x	Median	Mean	SD	CV%	n_{QL}	Comments
1 HPLC as sum of fractions	13	0	0.9	0.9	0.5	51.4	6	
2 Fluorescence spectroscopy	17	0	1.9	1.8	0.8	44.7	11	
0 Other	1	0	1.1	1.1			1	
All centres	31	0	1.1	1.4	0.8	56.6	18	

n: results included, n_x: results excluded from calculations, n_{QL}: results within method-related performance specifications.

Zinc/Metal-free protoporphyrin [%] reported by 29 out of 38 laboratories *

Porphyrin	n	n_x	**Your result**	Median	Range	Mean	SD	Comments
Zinc protoporphyrin	29	0	**71**	57	15 -100	59	17.1	
Metal-free protoporphyrin	29	0	**29**	43	0 - 85	41	17.1	

* The statistical calculations include results from method group 1 (HPLC as sum of fractions; n=11) and method group 2 (fluorescence spectroscopy incl. hematofluorimeter; n=18).

Enzyme activity [percent of lower value of reference range] reported by 21 out of 38 laboratories *

	n	n_x	**Your result**	Median	Range	Mean	SD	CV%	Comments
Porphobilinogen deaminase activity	20	0	**195**	189	71 - 294	177	51.4	29.0	
Uroporphyrinogen decarboxylase activity	9	0	**NA**	117	91 - 169	121	27.1	22.3	

* The statistical calculations include results from both method groups. For measurement of porphobilinogen deaminase activity 3 centres used HPLC (group 1) and 17 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).

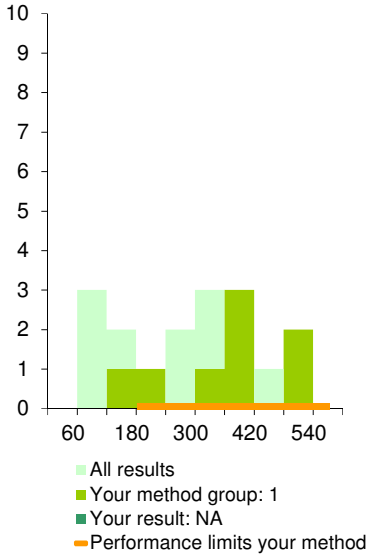
DNA analysis reported by 12 out of 38 laboratories

Nine centres sequenced the UROD gene without identifying any causative mutations, of these one also sequenced the UROS gene with a negative result. In addition, one centre sequenced the CPOX gene with a negative result and two centres examined the HFE gene and identified the C282Y/H63D genotype. Of these, one also reported a negative result for a commonly occurring mutation in the PPOX gene.

You reported:

Total plasma porphyrins [nmol/L] reported by 19 out of 38 laboratories

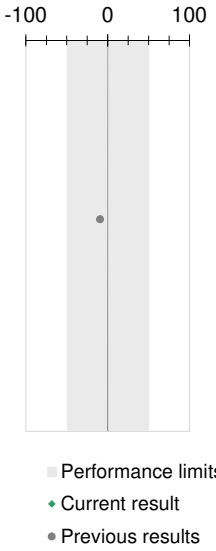
Histogram



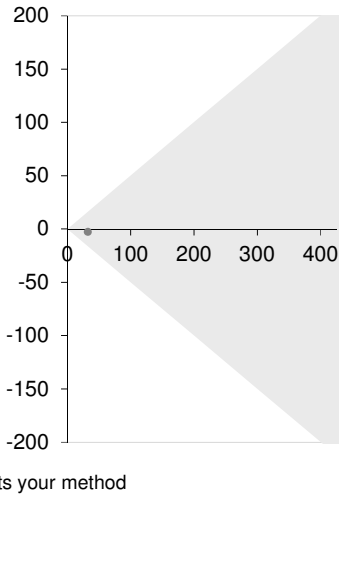
Historical data:

Survey	Median	Your result	Dev.%
2/18	379	NA	NA
1/18	26.0	NA	NA
2/17	25.0	NA	NA
1/17	88.9	NA	NA
2/16	185	NA	NA
1/16	32.6	29.6	-9.1
2/15	–	NA	NA
1/15	–	NA	NA
2/14	–	NA	NA
1/14	–	NA	NA
2/13	–	NA	NA
1/13	–	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	2	379	354	124	35.1	7	
2 Spectroscopy without HPLC	9	0	251	227	134	58.9	5	
0 Other	0	0	–	–			0	
All centres	17	2	324	287	141	49.3	12	

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

p-porphyrin fractions [%] reported by 11 out of 38 laboratories *

Porphyrin	n	n_X	**Your result**	Median	Range	Mean	SD	Comments
Uro total	9	2	**NA**	54	46 - 70	55	7.4	
Uro I	7	2	**NA**	44	39 - 57	47	8.1	
Uro III	7	2	**NA**	10	4 - 15	10	4.7	
Hepta	9	2	**NA**	28	23 - 39	29	6.4	
Hexa	8	2	**NA**	10	0 - 14	9	4.5	
Penta	8	2	**NA**	5	2 - 10	5	2.6	
Copro total	9	2	**NA**	1	0 - 9	2	2.7	
Copro I	7	2	**NA**	1	0 - 2	1	0.8	
Copro III	7	2	**NA**	0	0 - 7	1	2.5	
Proto	9	2	**NA**	2	0 - 4	2	1.3	

* The statistical calculations include only the results in method group 1 (HPLC; n=11).

Plasma scan [number of centres] reported by 33 out of 38 laboratories

Method group	n	Negative results	Inconclusive results	Positive results with emission peak at			Comments
				615 - 623[1]	> 623[2]	NC / NG	
1 (with rs-PMT/CCD)	23	0	0	22	1	0	
2 (without rs-PMT)	5	0	0	5	0	0	
3 (unknown PMT)	5	0	0	5	0	0	
All centres	**33**	**0**	**0**	**32**	**1**	**0**	
Your result; method gr. 1				618			

[1] For a PCT patient a positive plasma fluorescence scan with emission peak < 623 nm is expected.

[2] One laboratory reported emission wavelength at 632 nm.

Plasma ALA and PBG reported by 3 out of 38 laboratories

Two centres reported p-ALA results of 13 500 and 0 nmol/L.
Three centres reported p-PBG results of 500, 50 and 4 nmol/L.
Five centres reported having a method for p-ALA/PBG analysis.

Your result:

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	37	0	**0.5**	0.5	0.1 - 1.0	0.5	0.2	32.5	
u-PBG	37	0	**0.0**	0.2	0.0 - 1.0	0.3	0.2	73.0	
Total u-porphyrin	33	0	**35.6**	22.8	0.2 - 78.7	26.1	17.8	68.2	
Total f-porphyrin	26	1	**NR**	2.0	0.4 - 6.4	2.2	1.5	68.5	
Total e-protoporphyrin	28	0	**0.6**	0.9	0.2 - 2.6	1.0	0.6	57.9	
Total p-porphyrin	14	1	**NA**	16.8	3.4 - 35.3	16.9	9.0	53.5	

Diagnostic strategy for this case history reported by 38 out of 38 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	**–**	17	7	0	14	
u-PBG (quantitative)	**–**	18	7	0	13	
u-PBG (qualitative)	**–**	7	0	0	31	
Total u-porphyrin	**1**	27	4	0	7	
u-porphyrin fractionation	**2**	15	19	1	3	
u-uroporphyrin isomers	**–**	4	4	2	28	
u-other analyses	**–**	0	0	0	38	
Total f-porphyrin	**–**	14	15	1	8	
f-porphyrin fractionation	**1**	8	21	4	5	
f-coproporphyrin isomers	**–**	3	15	2	18	
f-other analyses	**–**	0	0	0	38	
Total e-proto-porphyrin	**–**	11	7	3	17	
Zinc proto-porphyrin	**–**	10	5	2	21	
Metal-free protoporphyrin	**–**	6	4	2	26	
other whole blood	**–**	0	0	0	38	
p-fluorescence scan	**1**	30	4	0	4	
p-ALA/PBG	**–**	1	1	0	36	
Total p-porphyrin	**–**	4	7	0	27	
p-porphyrin fractionation	**2**	2	4	2	30	
p-other analyses	**–**	0	0	0	38	
Uro-decarboxylase[1]	**–**	0	7	8	23	
UROD gene[2]	**3**	0	3	14	21	

[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] One centre also selected porphobilinogen deaminase as second-line. Two centres only selected porphobilinogen deaminase (scored 2) or uroporphyrinogen III synthase (scored 3), respectively.

[2] One centre also selected the UROS gene as third-line, and one PPOX gene as first-line. In addition, two centres only selected the UROS gene (scored 3) or CPOX gene (scored 2), respectively.

Requesting routines

Thirty-four laboratories provided information on requesting routines. Fourteen laboratories reported that they alone decide what analyses are to be performed, six that the requesting physician alone decides and 14 that both decide.

Laboratory report score

A laboratory report was submitted from 32 of the 38 centres. Twenty-two of the reports included all the 15 criteria, nine reports fulfilled from 12 to 14 criteria, and one report scored less than 10 points.
Date of arrival/registered and name/signature of verifying/responsible were the criteria most often lacking, followed by date of sampling, laboratory contact details, date of report, patient date of birth/ID, interpretation of results given and advice on further testing if appropriate and name of referring doctor/report destination.
The laboratory name, patient name, material tested, analyses performed, results, units and reference intervals were included in all the reports.
Reports written in languages we do not master may not be optimally scored. Please notify us if we have scored your laboratory report wrongly, so that this can be corrected in future surveys.

Your score:
Your attached laboratory report achieved 15 points.

Conclusion

You correctly diagnosed this case as sporadic PCT.

Other comments

Appendix

Clinical case history 2/18

Male born 1944 with bullae and fragile skin consistent with porphyria. Please provide recommendations for treatment and follow-up.

Sample data relevant for EQAS Survey 2/18

Urine creatinine: 11.8 mmol/L Haematocrit: 43 % Haemoglobin: 14.4 g/dL Reticulocyte count: 0.093 $x10^{12}$/L

Method groups 2/18

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:
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: Quantitative determination of porphyrins
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:
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
For porphyrins in plasma:	nmol/L

Appendix continued

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/reported	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 performance specifications

Analytical performance specifications

Analytical performance 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 performance 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 analytical performance specifications used are given for each analyte in the table below.

Limits of acceptable deviation from method median; desirable analytical performance	
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 v1/2003. 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.

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