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# Cognitive AA pilot scheme – Circulation 2018-2 - Participants Report

Participants were able to view the cases and submit their results using the ERNDIM Formdesk web site.

## Scoring system

During the evaluation of the current results, the four assessors came to the conclusion that since no actual analysis is performed, the scores for analytical findings were overvalued in relation to the other cognitive aspects. Therefore it was decided to score each of the three aspects, analytical findings, diagnosis and further tests, equally with two points each and also to keep the possibility of scoring with half points.

## Case 2018-4

### Arginase deficiency

The results provided were from a 1 month old boy, full term normal delivery who presented initially with vomiting, infection of the upper airways and became somnolent. Increased ammonia was found (307 µmol/L). After transfer to our hospital, sodium benzoic acid, glucose and hemofiltration were started. After this first episode the patient was stable, and has developed normally.
Plasma, CSF and urine amino acid concentrations together with the laboratories reference ranges were provided. The diagnosis of arginase 1 deficiency was made on the basis of the amino acid abnormalities and confirmed by the finding of compound heterozygosity for two mutations (c.647_648ins32 and c.871C>T in the *arginase 1* gene.

**Correct findings / abnormalities:**
Increases of plasma arginine (0.5), urinary arginine with ornithine and lysine (0.5) and CSF arginine and glutamine (1) were considered necessary for full points.

**Correct Diagnosis:**

The correct diagnosis was arginase deficiency scored with 2 pts. If another incorrect diagnosis was also mentioned, e.g. neonatal cystinuria (1 lab) or lysinuric protein intolerance (8 labs) only one point was given. Lysinuric protein intolerance or cystinuria alone were considered incorrect.

**Further tests:**

Measurement of blood ammonia (0.5) and urine orotic acid (0.5) were needed. Confirmation of diagnosis by arginase activity (1) and/or *ARG1* gene mutation (1) were correct.

**Comments on overall performance:**
Overall proficiency was fairly satisfactory at 87%. Performance for diagnosis and further test recommendations were slightly lower than for abnormalities.

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**Case 2018-5**

**Propionic acidemia**

**Sample details:**

After an uneventful birth, with normal pregnancy except that the mother suffered two seizures with normal EEG, the male patient became somnolent at the age of 10 days. On the same day results of newborn screening became available showing elevated propionyl-carnitine of 17 µmol/L (reference < 5)). Ammonia was elevated at 134 µmol/L. Investigation of organic acids in urine confirmed propionic acidemia. Treatment with glucose and L-carnitine led to prompt recovery. The patient is now 12 years old and remains in a good condition.

Plasma and urine amino acid concentrations together with the laboratories reference ranges were provided and the initial blood ammonia level were provided.

**Correct findings / abnormalities**:

Increased plasma glutamine (0.5), milder increase of glycine and alanine (0.5), a moderate increase of urinary glycine (0.5) and mild hyperammonemia (0.5) were considered necessary for full points.

**Correct Diagnosis**
Although the exact diagnosis was not possible, ketotic hyperglycinemia or propionic acidemia, or methylmalonic acidemia mentioned in the differential diagnosis was scored with 2 points.

**Further tests:**
Measurement of urine organic acids / acylcarnitines was considered to be the essential further test (2). Repeat plasma ammonia or FBC (0.5)

**Comments on overall performance**:
Performance was fairly good with 81% overall proficiency. The score for diagnosis was relatively low reflecting the non-specific findings.

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**Case 2018-6**

**Tyrosinemia type 3**

**Sample details**:

The sample was from an 11 year old male born at full term with normal pregnancy, birth weight and no family history.
The patient had recently moved to the UK having shown developmental delay from 4 months with and learning difficulties and poor coordination.
Further investigation showed motor skills on the 2nd centile. There were no painful lesions in toes/fingers and no corneal pain.
Organic acids analysis revealed raised phenolic acids with no succinyl acetone.
DNA analysis showed a homozygous deletion of *HPD* gene

Plasma amino acid levels with reference ranges were provided.

**Correct findings / abnormalities:**

A marked increase of plasma tyrosine received one point. It was important to note that methionine and phenylalanine were within the reference range since this argues against tyrosinemia type 1 and this received 1 point.

**Correct Diagnosis**

In view of clinical details, isolated increase in tyrosine and magnitude of the increase, mention of tyrosinemia type 2 or type 3 was considered correct. Mention of tyrosinemia type 1 in addition was penalised by 0.5 pt. (3 labs); only type 1 or 2 scored 1 point (2 labs); unspecified tyrosinemia (4 labs) scored 1 point and drug interference scored 0.5 pt.

**Further tests:**

Urine organic acids for succinyl acetone and phenolic acids scored 1 point. Mutation analysis for tyrosinemia type 2/3 was correct (1).

AFP or LFTs to receive 0.5 pt,

**Comments on overall performance:**

Overall proficiency was fairly good at 79% but would have been much higher except for low scores on abnormalities due to failure to mention normal methionine and phenylalanine.

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## Comments on the whole of the third circulation results

As mentioned above abnormalities, diagnosis and further tests were each scored with two points and half points were used again to allow more flexibility in the evaluation.
Each of the four evaluators scored all results independently and where four or three of their scores were in agreement, this was taken as final. In cases where such agreement was missing further close evaluation based on agreed scoring criteria was used to decide on the final score.
Generally cases were more difficult than in the 2017 circulation and there was a clear trend towards better performance for analytical findings than for interpretative aspects but more experience is needed to draw concrete conclusion on this.

*We encourage participants to send us comments and suggestions regarding this scheme and do not hesitate to contact us if you question any of our scoring.*

Date: 31.12.2018.

The Scientific evaluators:

Rachel Carling, Mary Anne Preece, Sabine Scholl-Bürgi and Brian Fowler

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| Lab I.D. | Sample 2018-4-Scores | | | | Sample 2018-5-Scores | | | | Sample 2018-6-Scores | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Abnormal 2 pts | Diag 2 pts | Tests 2 pts | **Total** | Abnormal 2 pts | Diag 2 pts | Tests 2 pts | **Total** | Abnormal 2 pts | Diag 2 pts | Tests 2 pts | **Total** | **Total** |
| 1 | 2 | 1 | 2 | **5** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **16** |
| 2 | 2 | 0 | 1 | **3** | 2 | 0 | 1 | **3** | 1 | 2 | 2 | **5** | **11** |
| 3 | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **17** |
| 4 | 2 | 2 | 2 | **6** | 2 | 1 | 2 | **5** | 1 | 1 | 1 | **3** | **14** |
| 5 | 2 | 2 | 2 | **6** | 1.5 | 2 | 2 | **5.5** | 1 | 2 | 2 | **5** | **16.5** |
| 6 | 2 | 2 | 2 | **6** | 2 | 0 | 2 | **4** | 2 | 2 | 2 | **6** | **16** |
| 7 | 2 | 2 | 1.5 | **5.5** | 1.5 | 2 | 2 | **5.5** | 1 | 2 | 2 | **5** | **16** |
| 8 | 2 | 2 | 1.5 | **5.5** | 1.5 | 2 | 2 | **5.5** | 2 | 2 | 2 | **6** | **17** |
| 9 | 2 | 2 | 2 | **6** | 2 | 0 | 2 | **4** | 1 | 2 | 1 | **4** | **14** |
| 10 | 1.5 | 2 | 1 | **4.5** | 1.5 | 2 | 2 | **5.5** | 1 | 2 | 1 | **4** | **14** |
| 11 | 1.5 | 2 | 0.5 | **4** | 1.5 | 2 | 2 | **5.5** | 2 | 1 | 1 | **4** | **13.5** |
| 12 | 2 | 2 | 1 | **5** | 1 | 0 | 0 | **1** | 1 | 2 | 2 | **5** | **11** |
| 13 | 1.5 | 2 | 1 | **4.5** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **15.5** |
| 14 | 2 | 1 | 2 | **5** | 2 | 2 | 0 | **4** | 1 | 2 | 2 | **5** | **14** |
| 15 | 2 | 0 | 1.5 | **3.5** | 1.5 | 0 | 1 | **2.5** | 1 | 1 | 1 | **3** | **9** |
| 16 | 2 | 2 | 1 | **5** | 2 | 2 | 2 | **6** | 2 | 2 | 1 | **5** | **16** |
| 17 | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **17** |
| 18 | 2 | 2 | 2 | **6** | 2 | 0 | 2 | **4** | 1 | 1 | 1 | **3** | **13** |
| 19 | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | **18** |
| 20 | 2 | 2 | 1.5 | **5.5** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **16.5** |
| 21 | 1.5 | 2 | 1.5 | **5** | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | **17** |
| 22 | 2 | 2 | 2 | **6** | 1 | 0 | 2 | **3** | 1 | 2 | 2 | **5** | **14** |
| 23 | 1.5 | 2 | 2 | **5.5** | 1.5 | 0 | 0 | **1.5** | 1.5 | 2 | 2 | **5.5** | **12.5** |
| 24 | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | 1 | 0.5 | 1 | **2.5** | **14.5** |
| 25 | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | 1 | 1.5 | 1 | **3.5** | **15.5** |
| 26 | 1.5 | 2 | 1.5 | **5** | 2 | 0 | 0 | **2** | 2 | 1.5 | 1 | **4.5** | **11.5** |
| 27 | 1.5 | 1 | 2 | **4.5** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **15.5** |
| 28 | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **17** |
| 29 | 2 | 1 | 2 | **5** | 1.5 | 0 | 0.5 | **2** | 1.5 | 2 | 2 | **5.5** | **12.5** |
| 30 | 2 | 2 | 1.5 | **5.5** | 2 | 2 | 2 | **6** | 2 | 2 | 1 | **5** | **16.5** |
| 31 | 2 | 2 | 1.5 | **5.5** | 2 | 2 | 2 | **6** | 1 | 1 | 2 | **4** | **15.5** |
| 32 | 2 | 2 | 2 | **6** | 1.5 | 2 | 2 | **5.5** | 1 | 2 | 1 | **4** | **15.5** |
| 33 | 2 | 2 | 2 | **6** | 2 | 0.5 | 0 | **2.5** | 2 | 2 | 2 | **6** | **14.5** |
| 34 | 1.5 | 1 | 2 | **4.5** | 1 | 0 | 2 | **3** | 1 | 2 | 2 | **5** | **12.5** |
| 35 | 2 | 2 | 2 | **6** | 1.5 | 2 | 2 | **5.5** | 1 | 2 | 2 | **5** | **16.5** |
| 36 | 2 | 1 | 2 | **5** | 1.5 | 2 | 2 | **5.5** | 1 | 2 | 2 | **5** | **15.5** |
| 37 | 2 | 2 | 1.5 | **5.5** | 2 | 2 | 2 | **6** | 1 | 2 | 1.5 | **4.5** | **16** |
| 38 | 1.5 | 2 | 2 | **5.5** | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | **17.5** |
| 39 | 2 | 2 | 2 | **6** | 2 | 2 | 2 | **6** | 1 | 1 | 2 | **4** | **16** |
| 40 | 2 | 0 | 0 | **2** | 2 | 2 | 2 | **6** | 1 | 2 | 2 | **5** | **13** |
| 41 | 1 | 2 | 1.5 | **4.5** | No scores submitted* | | | | | | | | **4.5*** |
| 42 | 2 | 1 | 1.5 | **4.5** | 2 | 2 | 2 | **6** | 1 | 1.5 | 2 | **4.5** | **15** |
| **Total** | 78.5 | 71 | 70 | 219.5 | 73.5 | 57.5 | 68.5 | 199.5 | 52 | 73 | 69.5 | 194.5 | |
| **% prof.** | 93 | 85 | 83 | 87 | 89 | 70 | 83 | 81 | 63 | 89 | 85 | 79 | |