Uncertainty in laboratory results using evidence from the Diagnostic Proficiency Testing scheme

Joanne Croft
DPT Scheme Organiser
Sheffield Children's NHS Foundation Trust

Overview

- What is the Diagnostic Proficiency testing scheme?
- How it is scored?
- What sort of errors do laboratories make?
- Take home message
- Plea for samples!!!!

Diagnostic Proficiency Testing Scheme

- ERNDIM Diagnostic Proficiency Testing (DPT)
- 5 centres (UK, Czech Republic, France, Netherlands, Switzerland)
- 19 – 23 participants per centre
- 6 urine samples sent to participants each year, 1 common to all schemes
- Clinical details provided – including if sample collected while on treatment

Report format

Participating laboratories decide which tests to perform based on the clinical information – not enough sample to perform every test

Report back analytical findings and conclusions reached

Investigations

pre-investigation (quantitative and qualitative results: pH, protein, glucose, creatinine, urate, etc.)

amino acids

organic acids

mucopolysaccharides

other assays e.g. purines/pyrimidines, oligos., acylcarnitines

Conclusion

Diagnosis, the probability of an enzyme deficiency

Advice for further investigation

Advice for the attending clinician

Scoring

A	Analytical Performance	Correct results of the appropriate tests	2
		Partially correct	1
		Unsatisfactory or mis-leading	0
I	Interpretation of results	Diagnosis established	2
		Helpful but incomplete	1
		Misleading/incorrect diagnosis	0

Maximum obtainable *24 points*

No return *0 points*

All scores awarded are moderated by a second DPT scientific advisor

Scoring and Critical Errors

- As from 2014 the ERNDIM DPT scheme issues critical errors
  - A critical error is an error that would be unacceptable to the majority of labs (>95%) and would have a serious adverse effect on patient management.
- Laboratories who otherwise obtain an acceptable score but who get a critical error are automatically sent a performance support letter
- What constitutes a critical error is decided at the ERNDIM Scientific Advisory Board meeting

Performance Support

- ERNDIM EQA schemes contain a large educational aspect

- The aim of the Performance Support letters are to open a dialogue with laboratories to solve any analytical problems and to improve performance.

What kind of errors are made?

- All results produced by the laboratory are subject to a degree of error
  - sample preparation (pre-analytical)
  - analyser error (analytical)
  - interpretation and reporting (post-analytical)
- There is evidence of these kind of errors from the DPT scheme

Evidence of Error - Example 1

Cystathionine beta synthetase deficiency

- Common sample sent to all DPT participants in 2015 – 107 laboratories
- 106 laboratories performed amino acid analysis
  - 101 reported increased homocystine
    - Median = 35 mmol/mol creatinine, range = 0.015 – 175
  - 66 reported increased methionine
  - 20 reported on the presence of the mixed cys-hcy disulphide

Evidence of Error - Example 1

- Possible diagnoses provided included:
  - CBS deficiency
  - homocystinuria
  - MTHFR deficiency
  - cobalamin defect
  - remethylation defect
- 7 laboratories did not provide any of these diagnoses

  (1 of these measured increased homocystine but stated that further investigation was required without providing any further guidance)

- Example of incorrect/incomplete analytical results

Evidence of Error - Example 2

Failure to detect orotic acid (2 cases)

Case 1

- 2015 UK scheme - 2/23 laboratories failed to identify argininosuccinic acid and orotic acid in a sample from a patient with argininosuccinic aciduria

Case 2

- 2014 UK scheme - HHH sample badly done – only 4/21 laboratories scored 4 marks
- 4/21 laboratories failed to detect orotic acid
- 17/21 laboratories failed to detect homocitrulline!
- This is particularly worrying as often we only receive a urine sample in the laboratory

- Examples of incorrect/incomplete analytical results

Evidence of Error - Example 3

Ethylene glycol ingestion

- Clinical details – ‘vomiting and unexplained metabolic acidosis’
- 21/22 laboratories identified increased glycolate with/without oxalate
- 19/22 laboratories considered most likely diagnosis to be ethylene glycol ingestion
- 2/22 laboratories diagnosed primary hyperoxaluria without considering ethylene glycol ingestion as a possible diagnosis*
- The remaining laboratory did not identify the key metabolites and reported a lactic acidosis. They did however state that an intoxication cannot be ruled out due to the 'unknown metabolites present' on their organic acid trace.

- *Example of correct analysis with incorrect interpretation

Evidence of Error - Example 4

Hartnups

- 20/20 laboratories correctly noted increased neutral amino acids in this sample
- 15/20 participants correctly diagnosed Hartnup disease
  - 5 labs noted that excretion of proline was not raised
- Of the remaining 5 participants who did not give Hartnup as a diagnosis:
  - 1 lab suggested maple syrup urine disease
  - 1 reported that the amino acid results suggested faecal contamination of the sample
  - 1 laboratory was unable to provide a diagnosis although they did state that the amino acids were abnormal
  - 1 laboratory suggested this was from a urea cycle disorder patient on treatment
  - 1 gave MPS type 3 as their primary diagnosis
- Example of correct analysis with incorrect interpretation

Take Home Message

- Just because we use hi-tech equipment does not mean we always get the correct result!
- Even if the analytical result is accurate it may not be interpreted correctly
- As a clinician – if the result you get back does not fit with the clinical picture – query the result with the laboratory and consider repeating the analysis

Plea for samples!!!

- We require real patient urine samples to run the DPT and organic acid schemes
- We will be unable to run these schemes without your immediate help
- For the DPT scheme we require 200ml urine/sample
- For the organic acid scheme we require 250ml of urine/sample
- Please contact us to discuss any samples you feel are suitable – anything which can be diagnosed from tests performed on urine.

- joanne.croft@sch.nhs.uk
- jane.dalley@sch.nhs.uk

- 0114 2717307