7 DEHYDROCHOLESTEROL

Relevant disorders

Smith Lemli Opitz syndrome

Indication for Test

The penultimate precursor of cholesterol this sterol accumulates in blood and tissues due to a deficiency of a 7-dehydrocholesterol-Δ-4-reductase. This gives rise to Smith-Lemi-Opitz syndrome characterised by microcephaly, facial dysplasia, growth and mental retardation as well as heart and kidney defects.
(NB 7-dehydrocholesterol also accumulates in CTX patients due to up-stream increase in cholesterol precursors).

Clinical findings include: Microcephaly, micrognathia, anteverted nostrils, ptosis, syndactyly of 2nd and 3rd toes, genital malformations in boys. Intellectual disability.
Very variable severity ranging from intra-uterine death to normal life span.

Methodology

Any esterified plasma sterols are hydrolysed by alkali in ethanol at 55^{o}C. The free sterols are then extracted into heptane and after drying are converted into trimethylsilyl (TMS) ethers for analysis by GCMS. An analogue internal standard (coprostanol or 5B-cholestan-3B-ol) is used for quantitation. Calibration curves are constructed for cholesterol, cholestanol and 7-dehydrocholesterol – standards are run with each assay. A separate qualitative analysis is used to detect any other abnormal plasma sterols such as desmosterol, lathosterol, and lanosterol.

Sample requirements

1 ml Lithium heparin blood, separate and send plasma.
Amniotic fluid for prenatal diagnosis (contact the laboratory prior to collection).

Transport information/Contact details

Send all samples by first class post to:

Department of Clinical Chemistry
Sheffield Children's NHS Foundation Trust
Western Bank, Sheffield
S10 2TH, UK

Joanne Croft (Clinical Scientist)
0114 2717307

Turn Around Time

4 weeks (but if requested urgently can be performed more quickly)

Reference Ranges

7-Dehydrocholesterol
Less than 2 µmol/L

Reported [Normal 0.1 - 0.6 µmol/L]
[Affected 5.2 - 1221 µmol/L]
(Ref: Kelley and Kratz Paed. Res. 37.No5.671-675.1995

References

- Kelley and Kratz Paed. Res. 37. No5. 671-675.1995
- Smith DW et al A newly recognised syndrome of multiple congenital anomalies (1964) J.Pediatrics Vol 64 no.2 210-217
- Clayton PT Disorders of cholesterol biosynthesis (1998) Arch Dis Child 78: 185-189
- Jira PE et al Pitfalls in measuring plasma cholesterol in the Smith-Lemli-Opitz syndrome. (1997) Clinical Chemistry 43:1 129-133