

Organisation of Laboratory Testing

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Mitochondrial Disease

- **Any organ**
- **Any age**
- **Any mode of inheritance**

Where on earth do we begin?

Clinical history

- **A recognisable syndrome eg MELAS**
- **An unexplained association of apparently unrelated pathologies**
- **Key laboratory findings eg elevated CSF lactate**
- **Suggestive family history**
- **Suggestive findings from other investigations eg MRI**

Markers of multi-system disease

- **CK, myopathy**
- **LFT's, liver disease**
- **Urinary aminoacids, renal tubular acidosis**
- **Endocrine investigations**

Specific metabolite abnormalities

- Lactate, CSF, plasma, urine
- Lactate:pyruvate ratio
- 3-hydroxybutyrate:acetoacetate ratio
- Intermediary metabolites, lactate, 3-hydroxybutyrate, pre- and 1 hour post prandial
- Urate, a reflection of chronic lactic acidaemia
- Urinary organic acids, TCA cycle intermediates, 3-methylglutaconate

Functional tests

- **Fat oxidation in vitro**
- **Allopurinol loading, urea cycle function**

DNA analysis

- **mt DNA, common mutations, sequencing**
- **Nuclear DNA, mutations**
- **Depletion**

Histopathology

- **Ragged red fibres**
- **Histochemistry**
- **Electron microscopy**

Respiratory chain enzyme measurement

- **Individual complexes**
- **Polarography of intact mitochondria**

Multidisciplinary review

- **Paeditrician**
- **Radiologist**
- **Biochemist**
- **Histopathologist**
- **Molecular geneticist**
- **Neurologist**
- **Clinical geneticist**