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## PAEDIATRIC HYPOGLYCAEMIA INVESTIGATIONS

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Hypoglycaemia is defined as plasma glucose less than 2.5 mmol/L by laboratory analysis. It may have many causes including infection, endocrine abnormalities and inherited metabolic diseases. It requires investigation if it persists beyond one day post-natal age in term babies, or three days post-natal age in pre-term or small-for-dates babies, and in all older children. Very occasionally, it may be necessary to conduct a closely supervised fast (not more than 10 hours), with frequent measurement of ward meter blood glucose, to provoke hypoglycaemia. However, prolonged fasting may be dangerous in some disorders e.g. fatty acid oxidation defects.

### Procedure

While the infant / child is hypoglycaemic (blood glucose meter or laboratory glucose is less than 2.5 mmol/L), collect 3 mL blood into lithium heparin tubes and 0.5 mL blood into a fluoride oxalate tube. If possible phone to warn the laboratory before taking any samples. Send by vacuum tube or (if off-site) collect on ice and transport to the laboratory without delay. Collect the next urine specimen passed, using a urine collection bag, if necessary, minimum volume 2 - 3 mL, no preservative. Send to the laboratory as soon as possible.

### Interpretation

To discuss individual patient results please contact the Duty Biochemist.

Assay	Normal responses / Comments	Interpretation & Disorders
<b><u>Fluoride oxalate plasma</u></b>		
<b>Glucose</b>	Essential to confirm hypoglycaemia	<2.5 mmol/L
<b>Lactate</b>	Reference Ranges: Neonates 0.5 - 3.0 mmol/L Infants & Children 0.6 - 2.4 mmol/L Artefactual increase may occur if venous stasis during sampling	Lactate increased in: <b>Tissue hypoxia and primary lactic acidosis</b> eg disorders of gluconeogenesis, respiratory chain complexes, pyruvate dehydrogenase and glycogen storage disease Type I.
<b>Hydroxybutyrate &amp; FFAs</b>	FFA >1.0 mmol/L indicates significant activation of fatty acid oxidation. FFA:HOB ratio is <1 for most causes of hypoglycaemia (ratio calculation only valid if FFA >1.0 mmol/L).	FFA >1.0 mmol/L and FFA:HOB ratio >1 is suggestive of a <b>fatty acid oxidation defect</b> . <b>Hyperinsulinism</b> : both FFA and HOB are inappropriately low for hypoglycaemia.

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<b>Assay</b>	<b>Normal responses / Comments</b>	<b>Interpretation &amp; Disorders</b>
<b><i>Lithium heparin plasma (in priority order)</i></b>		
<b>Insulin (± C-peptide)</b>	<p>Patient must be hypoglycaemic at time of sampling.</p> <p>Insulin &lt;14 pmol/L indicates appropriate suppression.</p> <p>If exogenous insulin administration suspected, measure C-peptide also.</p>	<p>Detectable insulin (&gt;14 pmol/L) &amp; C-peptide when hypoglycaemic is consistent with <b>transient or persistent hyperinsulinism or insulinoma</b>.</p> <p>Increased insulin with low C-peptide indicates <b>exogenous insulin administration</b>.</p>
<b>Cortisol</b>	<p>Infants &lt; 3mo show poor cortisol response to hypoglycaemia (only 75% &amp; 50% infants have levels &gt;165 nmol/L &amp; &gt;270 nmol/L respectively).</p> <p>Infants &amp; children &gt; 6mo usually have cortisol &gt;400 nmol/L during hypoglycaemia.</p> <p>Infants aged 3-6mo may show intermediate responses.</p>	<p><b>Infants &lt; 3mo:</b></p> <p>If cortisol &gt;270 nmol/L, disorders of hypothalamic-pituitary-adrenal (HPA) axis are unlikely.</p> <p>If cortisol 165-270 nmol/L, check GH level.</p> <p>If cortisol &lt;125 nmol/L, may need further investigation for possible pituitary or adrenal disorders.</p> <p><b>Infants &amp; children &gt; 6mo:</b></p> <p>Cortisol &gt;400 nmol/L, excludes disorders of HPA axis.</p>
<b>Growth hormone</b>	<p>Ideally patient should be hypoglycaemic at time of sampling. Samples taken out with the hypoglycaemic episode may be lower.</p> <p>Approx 80% of neonates (&lt;1 month old) have GH &gt;11 ug/mL during hypoglycaemia</p> <p>Approx 70% of infants and children &gt;6 months old have GH &gt;3 ug/L.</p> <p>Infants 1-6 months old may show intermediate responses</p>	<p><b>Infants &lt; 1mo:</b></p> <p>GH level &gt;11 ug/L indicates GH insufficiency unlikely.</p> <p><b>Infants &amp; children &gt; 6mo:</b></p> <p>GH &gt;3 ug/L indicates GH insufficiency unlikely.</p> <p><b>Infants &amp; children 1-6 mo:</b></p> <p>May show intermediate responses.</p> <p>Children with responses below these values should undergo formal review of growth if there is clinical concern over GH insufficiency.</p>
<b>TSH &amp; Free T4</b>	<p>Do not need to be done during hypoglycaemia. See website for appropriate RefR.</p>	<p>Combination of low free T4 and low TSH consistent with <b>hypopituitarism</b>.</p>
<b>Testosterone</b>	<p><b>Only in males &lt; 4mo.</b> Need not be done during hypoglycaemia. See website for appropriate RefR.</p>	<p>In panhypopituitarism normal postnatal surge of the hypothalamic -pituitary-gonadal axis may be absent.</p>
<b>Amino acids</b>	<p>Preferably during hypoglycaemia</p>	<b>Amino acid disorders</b>

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<b>CK</b>	Preferably during hypoglycaemia	<b>Fatty acid oxidation disorders, mitochondrial disorders, glycogen storage disorders</b>
<b>Ammonia</b>	Preferably during hypoglycaemia	<b>Urea cycle disorders, organic acidurias, acute liver failure</b>
<b><u>Blood spot on newborn screening card (obtain from laboratory)</u></b>		
<b>Acyl-carnitine</b>	Preferably during hypoglycaemia. THIS IS NOT A SUBSTITUTE FOR URINE ORGANIC ACID ANALYSIS.	<b>Limited number of Long chain fatty acid oxidation disorders and Organic Acidurias.</b>
<b><u>First Urine passed following hypoglycaemic episode</u></b>		
<b>Organic acids</b>	<u>Must</u> be first urine sample passed following hypoglycaemic episode	<b>Wider range of Organic acid disorders, fatty acid oxidation defects and amino acid disorders.</b>
<b>Amino acids</b>		<b>Amino acid disorders</b>

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