ICE Test Name: Child CRH Stimulation (-15m)

Principle
CRH is normally released by the hypothalamus to stimulate ACTH release by the anterior pituitary. The administration of a CRH analogue (corticorelin) can therefore be used to assess the ability of the pituitary gland to secrete ACTH for the stimulation of cortisol production. Generally patients with pituitary ACTH deficiency have a decreased ACTH and cortisol response to CRH. Patients with hypothalamic disorders however have an exaggerated and prolonged plasma ACTH response and a subnormal cortisol response.

The CRH test may also be used in combination with dexamethasone suppression tests for the differential diagnosis of Cushing’s syndrome. CRH administration results in an excessive rise in plasma ACTH and serum cortisol in patients with pituitary Cushing’s disease, whilst this is rarely seen in patients with ectopic ACTH secretion. The CRH test can therefore be used in the differential diagnosis of Cushing’s syndrome to confirm whether the cause is pituitary-dependent or ectopic.

Indication
• To differentiate between pituitary-dependent and ectopic causes of Cushing’s syndrome.

Precautions
• Imipramine may reduce the ACTH response

Side Effects
• Flushing of the face, neck and upper body, hypotension or a mild sensation of taste or smell may occur following administration of CRH.

Preparation
• The patient should be fasted overnight (for a minimum of 4 hours).
• The patient should remain supine throughout the test.
• If the patient is to also have a high dose dexamethasone suppression test, the CRH test should be performed first.

Protocol
1. Insert a reliable cannula and wait 30 minutes before proceeding with the test.
2. Take a blood sample for ACTH and cortisol 15 minutes after the insertion of the cannula.
3. 15 min later: Administer CRH (corticorelin) i.v. at a dose of 1 microgram/kg body weight (to a maximum of 100 micrograms) over 30 seconds. Collect blood samples for ACTH and cortisol (t = 0).
4. Take further blood samples for ACTH and cortisol at 15, 30, 45, 60, 90 and 120 min post CRH administration.
Time Points:

<table>
<thead>
<tr>
<th>Time post CRH (min)</th>
<th>Procedure</th>
<th>Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>-15</td>
<td>-</td>
<td>Blood for Cortisol/ ACTH</td>
</tr>
<tr>
<td>0</td>
<td>CRH administration</td>
<td>Blood for Cortisol/ ACTH</td>
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<tr>
<td>15</td>
<td>-</td>
<td>Blood for Cortisol/ ACTH</td>
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<tr>
<td>30</td>
<td>-</td>
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<tr>
<td>45</td>
<td>-</td>
<td>Blood for Cortisol/ ACTH</td>
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<tr>
<td>60</td>
<td>-</td>
<td>Blood for Cortisol/ ACTH</td>
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<tr>
<td>90</td>
<td>-</td>
<td>Blood for Cortisol/ ACTH</td>
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<tr>
<td>120</td>
<td>-</td>
<td>Blood for Cortisol/ ACTH</td>
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</tbody>
</table>

Sample

ACTH
2-3 mL blood in a 5 mL lithium heparin tube (orange top)

Send IMMEDIATELY to laboratory on ice for centrifugation and freezing

Cortisol
1 mL lithium heparin (orange top) or clotted blood (white top)

Record the actual sample collection times on the printed barcodes

Interpretation

- A peak increment of serum cortisol >20% and plasma ACTH >50% suggests Cushing’s disease. The CRH test has a sensitivity of 86-93% and a specificity of 90-100% using these cut off values to discriminate Cushing’s disease from ectopic ACTH secretion.

- A rise in ACTH by 35% at 15 and 30 min compared to basal levels also suggests a pituitary source.

- The CRH test has been reported to show a high sensitivity in diagnosis of Cushing’s disease in pre-pubertal children.

- CRH is also used to aid bilateral petrosal sinus sampling. The diagnostic sensitivity of basal central/peripheral ACTH ratio >2 and >3 post CRH is 94%.

References

1. Nieman LK, Lacroix A, Martin KA. Corticotrophin-releasing hormone stimulation test. UpToDate April 2012