

Corticotrophin Releasing Hormone (CRH) Test - Full Clinical Guideline

Reference no.: CHISG8

**THIS TEST IS ONLY TO BE PERFORMED FOLLOWING ADVICE FROM A PITUITARY
NEUROSURGICAL CENTRE**

1. Introduction

Corticotrophin Releasing Hormone (CRH) is a 41 amino acid polypeptide produced from the hypothalamus. CRH stimulates the anterior pituitary corticotrophs to release Adrenocorticotrophin Hormone (ACTH). Most patients with pituitary-dependant Cushing's syndrome show a normal or exaggerated cortisol (and ACTH) response to CRH. Those with ectopic ACTH secreting tumors do not respond to CRH.

**CORTERELIN IS NOT A LICENSED PRODUCT AND IS FOR RESEARCH PURPOSES
ONLY, BUT IS APPROPRIATE FOR USE IN ACCORDANCE WITH THIS PROTOCOL**

2. Guideline

INDICATIONS

The CRH test is used in the differential diagnosis of Cushing's syndrome.

CONTRAINDICATIONS

This procedure should not be performed in patients with a history of allergy to Corterelin.

SIDE EFFECTS

Mild facial flushing may last up to 1 hour. Occasional shortness of breath, tachycardia and allergic reactions. Occasional marked transient hypotension was reported with previously used higher doses of Corterelin. Most patients get a metallic taste in the mouth shortly after injection.

PRECAUTIONS

Patient should be warned that flushing is likely. Patient should be closely monitored throughout the test.

PREPARATION

Planning

This procedure requires insertion of an indwelling venous cannula.

Patient

The patient should fast from midnight on the day prior to the test, and not smoke, eat or drink anything except tap water until the test is completed.

The patient should be at rest before and during the test. If the patient is taking corticosteroids, postpone the morning dose until after the test.

Equipment

- Corterelin/Corticotropin available as 100 micrograms per vial, obtainable from Pharmacy
- Indwelling venous cannula
- 6 SST tubes (yellow top)
- 6 EDTA tubes (purple top)
- 6 plastic syringes

PROCEDURE

Care must be taken to avoid haemolysis during venepuncture, as this invalidates the ACTH assay. Samples must be labelled clearly with patient name, date and time of sampling.

At each time point take 10 mL of blood using a plastic syringe and put 4 mL into a Purple top (EDTA) tube and the remainder into a SST tube (yellow top). **All samples can be sent to the laboratory together in a red bag at the end of the test.**

TIME	BLOOD SAMPLE for cortisol and ACTH
- 45 minutes (e.g. 08:15)	Insert the venous cannula and allow the patient to rest for 30 minutes
-15 minutes	5 mL blood in yellow top tube and 4 mL blood in purple top tube
Time = 0 (zero)	5 mL blood in yellow top tube and 4 mL blood in purple top tube
Immediately after time zero sample, give Corterelin/Corticotropin 100 µg iv bolus. (There are 2 vials which require mixing before administration)	
+ 15 minutes	5 mL blood in yellow top tube and 4 mL blood in purple top tube
30 minutes	5 mL blood in yellow top tube and 4 mL blood in purple top tube
45 minutes	5 mL blood in yellow top tube and 4 mL blood in purple top tube
60 minutes	5 mL blood in yellow top tube and 4 mL blood in purple top tube

INTERPRETATION

The utility of the test is in the differential diagnosis of ACTH dependant Cushing's Syndrome. The high dose dexamethasone suppression test is complementary to the CRH test and is usually performed in tandem.

In Cushing's disease there is typically a normal or exaggerated ACTH response to CRH, with rises of >50% of ACTH over baseline and >20% increment of cortisol over baseline. Note that 10-15% of patients do not respond to CRH, but do respond to the high dose dexamethasone suppression test.

In Cushing's Syndrome due to ectopic ACTH secreting tumours (when ACTH levels are typically very high) or adrenal tumours (when ACTH is suppressed), there is no ACTH response to CRH in 90% of patients. In the 10% of patients with ectopic ACTH who respond to a CRH test, there is no suppression with the high dose dexamethasone suppression test.

In depression the cortisol response may be normal with a reduced ACTH response.
In substantial obesity the cortisol response may be blunted.

REFERENCE RANGES (basal values)

Cortisol: 6am – 10am 166 - 507 nmol/L
 4pm – 8pm 74 - 291 nmol/L

ACTH: 7am – 10am 7.2 – 63.3 ng/L

TURNAROUND TIME

Cortisol results will normally be available within two working days following the test.

ACTH results are usually available within 3 weeks.

3. References

Newell-Price et al. Optimal response criteria for the human CRH test in the differential diagnosis of ACTH-dependant Cushing's syndrome. *J Clin Endocrinol Metab* 2002; 87: 1640-45.

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Grossman A *et al.* CRF in the differential diagnosis of the Cushing's syndrome : a comparison with the dexamethasone suppression test. *Clin. Endocrinol.* 1988; **29**: 167-178.

Trainer & Besser in *The Bart's Endocrine protocols*. Section 1 p 12-13.

4. Documentation Controls

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