

72 Hour Fast - Full Clinical Guideline

(Document Code: CHISCG35)

**THIS TEST IS ONLY TO BE PERFORMED FOLLOWING DISCUSSION WITH
A CONSULTANT BIOCHEMIST OR ENDOCRINOLOGIST**

1. Introduction

Hypoglycaemia in the absence of drugs that lower serum glucose (i.e. during treatment for diabetes mellitus), is a rare event. Symptoms compatible with hypoglycaemia are comparatively common. It is important to be able to identify the small proportion of people with these symptoms who have hypoglycaemia, especially those with fasting insulin excess (e.g. insulinoma).

Where possible it is important to confine investigations to those patients with Whipple's Triad:- symptoms or signs of hypoglycaemia, low serum glucose at the time of the attack and resolution of symptoms or signs after glucose concentration is raised. It is acknowledged that confirmation of low serum glucose may require formal investigation.

It is appropriate to focus testing on circumstances known to precipitate symptoms. The initial test for a patient with fasting symptoms is therefore a prolonged fast whereas the prolonged oral glucose tolerance test or mixed meal test is appropriate for most patients with daytime symptoms.

Guidance in this protocol is based on The Endocrine Society Clinical Guideline; 'Evaluation and Management of Adult Hypoglycaemia Disorders'.

Note; Critical illness can be associated with hypoglycaemia due to sepsis, hepatic, renal or cardiac failure- this test should not be used in these circumstances.

2. Guideline

INDICATIONS

Confirmation and differential diagnosis of suspected fasting hypoglycaemia.

CONTRAINDICATIONS

Hypoglycaemic drugs for diabetes
Severe acute illness, as above
Untreated adrenal insufficiency

SIDE EFFECTS

Nil, but test potentially unpleasant due to severe hunger

PRECAUTIONS

Exclude adrenal insufficiency- this will need cortisol measurement and often Short Synacthen Test with review of results prior to undertaking the fast.

PREPARATION

Discontinue all non-essential medications on day of commencing test- referring doctor to advise of medications to be omitted.

PROCEDURE**General**

Patient eats or drinks normally leading up to the test- including breakfast on the day of the test if wanted.

No food to be eaten during the test.

No calorie or caffeine containing drinks to be taken during the test.

Day & Time	Action	Extra bedside testing	Laboratory bloods
1 09:00 15:00 21:00	Check bedside blood glucose Check bedside blood glucose Check bedside blood glucose	Also check bedside blood sugar at any time when patient reports symptoms compatible with hypoglycaemia. Testing should be increased to every 2hrs when blood sugar levels drop to <3.3 mmol/L.	If capillary blood glucose <3.3 mmol/L send bloods to lab <u>urgently</u> for analysis. Send one yellow top and one grey top and request glucose, insulin, C-peptide and sample STORE.
2 03:00 09:00 15:00 21:00	Check bedside blood glucose Check bedside blood glucose Check bedside blood glucose Check bedside blood glucose		
3 03:00 09:00 15:00 21:00	Check bedside blood glucose Check bedside blood glucose Check bedside blood glucose Check bedside blood glucose	Do not end fast unless lab glucose confirmed <2.5 mmol/L when patient has symptoms or <2.2 mmol/L without symptoms	Phone the lab to check the glucose result before ending the test.
4 03:00	Check bedside blood glucose		

Fast ends when ANY of the following apply:

- Lab glucose is < 2.2 mmol/L
- Lab glucose is < 2.5 mmol/L and the patient is symptomatic or displaying signs of hypoglycaemia (e.g. includes confusion if hypoglycaemia unaware patient)
- 72 hours have elapsed since the start of the test
- Do not end the Fast on the basis of a bedside sugar test

Stopping the Fast:

Send **two** yellow tops and **two** grey tops and request glucose, β -hydroxybutyrate, insulin, C-peptide and sample STORE.

Then give 1 mg Glucagon iv.

10 min post injection Send grey top for glucose

20 min post injection Send grey top for glucose

30 min post injection Send grey top for glucose

Patient can now eat and drink as desired

Stopping the fast

The principle of the test is to induce hypoglycaemia and assess the patient's symptoms and biochemical response to the low blood sugar so it is important that the test is not terminated before this information can be derived. Exceptions to this would include where consciousness level drops or the patient develops chest pain suggestive of cardiac ischaemia in which case the test should be terminated without delay and an urgent medical review requested.

The Fast ends when any of the following apply;

1. **Laboratory** glucose is less than 2.2 mmol/L
2. **Laboratory** glucose is less than 2.5 mmol/L and the patient is symptomatic or displaying signs of hypoglycaemia (e.g. includes confusion if hypoglycaemia unaware patient)
3. 72 hours have elapsed since the start of the test

Do not end the fast on the basis of a bedside sugar test.

Regardless of the reason for stopping the Fast it is vital to send bloods before reversing hypoglycaemia. Send two yellow tops and two grey tops and request glucose, insulin, C-peptide, β -hydroxybutyrate and sample STORE. The lab will add on proinsulin or sulphonylureas only if appropriate after discussion with Consultant Endocrinologist.

If it is judged necessary to treat hypoglycaemia urgently due to severe or dangerous symptoms obtain samples as above and then administer carbohydrate (oral route if conscious, i.v. route if unconscious or chest pain).

After the last fasted sample is collected as above, give 1mg glucagon i.v. and measure send blood for glucose (grey top) after 10, 20 and 30 minutes. The patient can now eat and drink as desired. It is advisable to obtain the samples from the i.v. cannula during this part of the test in view of the frequency of testing required. Ensure that 5 - 10 mL of blood is discarded before the test sample is taken on each occasion in order to avoid contamination. Flush the line with a small volume of saline after each sample to maintain patency.

Analysis of samples

Samples will be stored in Biochemistry for potential further analysis which will depend on results. Proinsulin will only be measured in the subset of samples where glucose <3.3 mmol/L and results from overall 72 hour fast results are equivocal for endogenous insulin excess after discussion with Consultant Endocrinologist. Sulphonylureas and insulin antibodies will be measured if results suggest insulin excess (on single sample each). β -hydroxybutyrate will be measured on the last sample of the fast or when test terminated (needs second grey top tube).

INTERPRETATION

Table 2 represents expected results of all measured parameters for all relevant diagnoses.

Essentially a normal response to prolonged fasting may include hypoglycaemia (glucose <3mmol/L) but this should be accompanied by suppressed endogenous insulin production (insulin less than 20 pmol/L and C-peptide less than 200 pmol/L) and starvation appropriate ketogenesis (increased β -hydroxybutyrate). Glucagon response in the normal fasted patient is reduced due to depletion of glycogen stores which are inappropriately preserved in patients with insulin excess.

Glucose, insulin and C-peptide levels are often sufficient to exclude insulin excess but studies show a lack of clear cut off with any one investigation. Therefore the extra parameters can be helpful in borderline cases.

Table 2

Glucose (mmol/L)	Insulin (pmol/L)	C-peptide (pmol/L)	Pro-insulin (pmol/L)	β -hydroxy butyrate (mmol/L)	Glucose rise with glucagon (mmol/L)	Sulphonyl ureas	Antibody to insulin	Diagnostic interpretation
<3.0	<18	<200	<5	>2.7	<1.3	Negative	Negative	Not insulin mediated
<3.0	>18	<200	<5	<2.7	>1.3	Negative	Negative	Exogenous insulin
<3.0	>18	>200	>5	<2.7	>1.3	Negative	Negative	Insulinoma
<3.0	>18	>200	>5	<2.7	>1.3	Positive	Negative	Oral hypoglycaemic
<3.0	>18	>200	>5	<2.7	>1.3	Negative	Positive	Insulin autoimmune
<3.0	<18	<200	<5	<2.7	>1.3	Negative	Negative	IGF mediated

Application of Table 2 should allow diagnosis in the vast majority of cases. Appropriate further investigations, such as imaging, will depend on diagnosis.

TURNROUND TIME

Glucose, Insulin and C-peptide results are available within one working day.

Samples that have been requested to be stored are kept frozen for 3 months before being discarded. The decision to add on further tests to these samples must be made within this time. Proinsulin, β -hydroxybutyrate, sulphonylureas and insulin antibodies are not analysed at Royal Derby Hospital and results may take up to 3 weeks to return.

3. References

Evaluation and Management of Adult Hypoglycaemic Disorders
An Endocrine Society Clinical Practice Guideline, 2009, JCEM; 94: 709-728

4. Documentation Controls

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