

## Dynamic Endocrine Testing

Note: label lab requests and samples with the type of test and time relative to the administered medication e.g. "GTT, +30mins"

### Oral glucose tolerance test (for diabetes)

**Assesses for:** diabetes mellitus; impaired fasting glucose; impaired glucose tolerance

**Physiology:** a glucose load is given in order to stimulate insulin secretion – the glucose level in patients with reduced insulin secretion or insulin resistance will fail to return to normal

#### Preparation

- Patient fasted from midnight

#### Procedure

- 9am: take glucose level
- Give 75g of glucose (e.g. Polycal 122ml) orally within 5 minutes
- At 2 hours: take a second glucose level

#### Interpretation

- Diabetes: fasting glucose  $\geq 7$ mmol/L or 2-hour GTT glucose  $\geq 11.1$ mmol/L
- Impaired fasting glucose: fasting glucose 6.1-6.9mmol/L
- Impaired glucose tolerance: 2-hour GTT glucose 7.8-11.0mmol/L

### Oral glucose tolerance test (for acromegaly)

**Assesses for:** acromegaly

**Physiology:** a glucose load is given in order to suppress GH production – in patients with acromegaly, GH is secreted inappropriately and will not suppress

#### Preparation

- Patient fasted from midnight

#### Procedure

- 9am: take glucose + GH level + IGF-1
- Give 75g of glucose (e.g. Polycal 122ml) orally within 5 minutes
- Every 30 mins: take a second glucose + GH level
- Stop at 2 hours

#### Interpretation

- GH should be suppressed to  $< 0.3 \mu\text{g/L}$  in normal people – it is not suppressed in acromegaly

### Short Synacthen test

**Assesses for:** Addison's disease (adrenal insufficiency)

**Physiology:** synthetic ACTH is given in attempt to stimulate the adrenal gland to produce cortisol

**Contraindications:** pregnancy; previous hypersensitivity to Synacthen; within 6 weeks of pituitary surgery

**Risks:** anaphylaxis/hypersensitivity

#### Preparation

- If on oral contraceptive pill or HRT, stop this for 6 weeks pre-test (resume after test)
- If on prednisolone, change this to dexamethasone 2 weeks pre-test
- If on hydrocortisone/dexamethasone, stop it the evening before (resume after test)

#### Procedure

- 9am: insert cannula (take bloods from this throughout)
- Wait 15 minutes then take baseline cortisol  $\pm$  ACTH levels (take to lab urgently on ice if required)
- Give Synacthen 250mcg IV
- At 30 and 60 mins: take cortisol levels

#### Interpretation

- Normal result: cortisol  $> 420$ nmol/L at 30 mins
- Cortisol  $< 420$ nmol/L at 30 mins suggests adrenal insufficiency
- Cortisol rise of  $< 170$ nmol/L after 30mins suggests reduced adrenal reserve

## **Extended oral glucose tolerance test**

**Assesses for:** reactive hypoglycaemia

**Physiology:** a glucose load is given and the patient is monitored for hypoglycaemia – in patients with reactive hypoglycaemia, excess insulin is released after a carbohydrate load which results in hypoglycaemia within 4 hours of eating

**Risks:** hypoglycaemia

### Preparation

- Patient fasted from midnight

### Procedure

- 9am: insert cannula (take bloods from this throughout) and take glucose and insulin levels
- Check capillary glucose
- Give 75g of glucose (e.g. Polycal 122ml) within 5 minutes
- Every 30 mins: take glucose, insulin and C-peptide levels
- Take additional samples if the patient has hypoglycaemic symptoms and a capillary glucose of <4mmol/L
- Check capillary glucose after each sample
- Stop at 5 hours and give the patient a snack

*Note: blood samples must be taken urgently to lab so the insulin samples can be frozen*

### Interpretation

- Glucose  $\leq 3.5$  mmol/L is abnormal and indicates reactive hypoglycaemia

*Note: patients with reactive hypoglycaemia almost always spontaneously recover; patients with fasting hypoglycaemia do not recover until they have ingested carbohydrate*

## **72 hour fast**

**Assesses for:** cause of suspected fasting hypoglycaemia

**Physiology:** patient is subjected to prolonged fast which aims to trigger hypoglycaemia – when this occurs, blood is taken for insulin and C-peptide to determine the cause of hypoglycaemia

**Contraindications:** pregnancy, terminal disease, renal failure

**Risks:** hypoglycaemia

### Preparation

- Eat and drink normally until test starts

### Procedure

- Admit patient
- At start of fast, take blood for glucose, insulin and C-peptide
- Patient is only allowed caffeine-free and calorie-free drinks and their regular medications
- Perform capillary glucose measurements 6-hourly until <3.3mmol/L, then 2-hourly
- If ever the capillary glucose is <2.5mmol/L or patient is symptomatic, take blood for glucose, insulin and C-peptide
- Actions
  - If the lab glucose is ever confirmed to be <2.5mmol/L with symptoms (or <2mmol/L without) or the patient gets to 72 hours, terminate the test
  - At the end of the test take blood for beta-hydroxybutyrate (ketones should be suppressed in insulinoma due to excess insulin) and sulfonyleurea screen, and give patient a sugary drink and some long acting carbohydrate – then monitor capillary glucose every 10mins until >4mmol/L, then 2-hourly until 6 hours
  - If the patient requires emergency treatment for hypoglycaemia, it should not be withheld

*Note: patient is not allowed to leave the ward unaccompanied due to risk of hypoglycaemia and exogenous insulin administration*

### Interpretation

- Venous glucose <2.5mmol/L with symptoms (or <2mmol/L without) is significant
- If insulin is high (>3mU/L) and C-peptide is high (>200pmol/L), this suggests insulinoma
- If insulin is high (>3mU/L) and C-peptide is low (<75pmol/L), this suggests exogenous insulin administration
- If insulin is low (<3mU/L) and C-peptide is low (<75pmol/L), this is appropriate – seek alternative causes of hypoglycaemia (e.g. alcohol, adrenal insufficiency, hypopituitarism, liver failure, mesenchymal tumour etc.)

## Water deprivation test

**Assesses for:** diabetes insipidus

**Physiology:** patient is subjected to dehydration which normally stimulates the posterior pituitary to release ADH resulting in increased water retention in the kidneys and therefore concentrated urine

**Risks:** severe dehydration

### Preparation

- Patient nil by mouth from midnight
- If on DDAVP, stop it the evening before (resume after test)
- If on any anterior pituitary hormone replacement, these should be taken 1 hour before test

### Procedure

- Start at 9am
- Cannulate (take bloods from this throughout)
- At baseline (0 hours) and then every hour check:
  - Weight, BP and pulse
  - Urine output (they should hold urine until the hour is up) – weigh the urine in a bowl and then subtract the weight of the bowel
  - Send urine sample for urine osmolality
  - Take blood for serum osmolality and U&Es
- At 2pm, review results:
  - If normal (i.e. urine osmolality > 750nmol/kg), stop test
  - If abnormal, give 2mcg desmopressin IM or IV and continue test
- If urine osmolality >750nmol/kg, stop test

*Note: if patient loses >3% of bodyweight or serum osmolality is >305 or Na<sup>+</sup>>150, consider whether to stop test or give fluids and 2mcg desmopressin IM or IV (then continue with free fluids for 2 more hours)*

### Interpretation

- Hypertonic urine (>750nmol/kg) should occur in response to water deprivation and this indicates normality
- Hypotonic urine (<750nmol/kg) by 2pm despite water deprivation is abnormal
  - If the urine then becomes hypertonic (>750nmol/kg) after desmopressin, this indicates cranial diabetes insipidus as the kidneys still respond to ADH
  - If the urine remains hypotonic (<750nmol/kg) after desmopressin, this indicates nephrogenic diabetes insipidus because the kidneys are resistant to ADH
- Sub-maximum urine concentration (500 – 700 mmol/kg) with no response to desmopressin suggests compulsive drinking or partial nephrogenic DI

## Insulin stress test

**Assesses for:** GH and/or cortisol deficiency (in patients with pituitary/hypothalamic disease)

**Physiology:** insulin is used to induce extreme hypoglycaemia, during which GH and ACTH should be released as part of the stress mechanism

**Contraindications:** ischaemic heart disease; epilepsy

**Risks:** hypoglycaemia

### Preparation

- If on oral contraceptive pill, stop this for 6 weeks pre-test (resume after test)
- If on hydrocortisone, stop it the evening before (resume after test)
- Patient fasted from midnight

### Procedure

- Ensure medication is available if complications: glucose 20% infusion (10-20ml if patient becomes unconscious); glucagon 1mg IM; hydrocortisone 100mg injection (if patient appears hypoadrenal i.e. hypotensive and tachycardic)
- Patient should lie supine
- 9am: insert cannula (take bloods from this throughout)
- At 10mins: take basal cortisol, GH and glucose levels
- Give Actrapid insulin IV
  - Normal patient: 0.15units/kg
  - Hypopituitary patient: 0.1units/kg
  - Acromegalic/Cushing's/Diabetic patient: 0.3 units/kg
- Check pulse, BP
- Check capillary blood glucose every 15 mins
- If capillary glucose is not <2.2mmol/L in first 45 mins, give another half dose of insulin

- Once capillary glucose is  $<2.2\text{mmol/L}$  take blood samples for cortisol, GH and glucose levels at +0, 15, 30, 45, 60, 90 and 120 mins
- Check BP and pulse after each blood sample
- After 120min samples, give sugary drinks and 2 slices of toast with jam
- They can be discharged when capillary glucose is  $>4\text{mmol/L}$  and they have had the toast

#### Interpretation

- Test can only be interpreted in presence of hypoglycaemia ( $<2.2\text{mmol/L}$ )
- Cortisol should rise  $>170\text{nmol/L}$  to  $>500\text{nmol/L}$
- GH should increase to  $>7\mu\text{g/L}$  ( $<3\mu\text{g/L}$  = deficiency) – use peak value

### **Glucagon stimulation test**

**Assesses for:** GH and/or cortisol deficiency (if insulin stress test contraindicated)

**Physiology:** glucagon is given to stimulate the release of GH and ACTH

#### Preparation

- Patient fasted from midnight
- If on hydrocortisone, stop it the evening before (resume after test)

#### Procedure

- 9am: insert cannula (take bloods from this throughout)
- At 10mins: take basal cortisol, GH and glucose levels
- Give glucagon 1mg intramuscularly (1.5mg if  $>90\text{kg}$ )
- Every 60 mins: take blood from cannula for cortisol, GH and glucose levels
- Stop at 4 hours

#### Interpretation

- Cortisol should rise  $>170\text{nmol/L}$  to  $>500\text{nmol/L}$
- GH should increase to  $>7\mu\text{g/L}$  ( $<3\mu\text{g/L}$  = deficiency) – use peak value

### **Cortisol day curve**

**Assesses for:** adequacy of hydrocortisone treatment or cortisol reserve

#### Preparation

- Patient should be told to omit the morning dose of hydrocortisone until the first blood sample has been taken

#### Procedure

- Cannulate (take bloods from this throughout)
- After 15mins, take blood for cortisol baseline
- Patient can then take usual morning dose of hydrocortisone if on it (record dose)
- Take cortisol level at 2 hours, then 4 hours, then patient can take lunchtime hydrocortisone dose (record dose)
- Take cortisol level at 6 hours, then 8 hours, then patient can take evening hydrocortisone dose (record dose)

#### Interpretation

- Optimal plasma cortisol is  $150\text{-}300\text{nmol/L}$