Scottish Paediatric Endocrine Group
Managed Clinical Network
(SPEG MCN)

Dynamic Function Test Handbook for Clinicians

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INTRODUCTION

This handbook is for clinicians managing children with endocrine disorders in Scotland, and sets out standard ways of performing dynamic function tests.

This is a consensus document of good practice and evidence where available. It has been collated by the Scottish Paediatric Endocrine Group MCN (SPEGMCN) Protocols sub-group.

This document is available in electronic form at:
www.endocrine.scot.nhs.uk

Levels of paediatric endocrine care:

The British Society for Paediatric Endocrinology and Diabetes (BSPED) has recently produced standards advising on 3 levels of paediatric endocrine care:

http://www.bsped.org.uk/clinical/docs/BSPEDPaediatricEndocrineStandardsvs130710.pdf

This handbook covers all 3 levels of care. In following the guidelines within, the clinician must be aware of the level of care which they can provide from their centre so should not enter in to the management of cases without understanding these advised standards. For example, although the protocol for the insulin tolerance test is described within this guide, this should only be carried out within centres that do it regularly i.e., more than 12 times per year.

If in doubt about the necessity or practicality of performing any of these tests in your local centre, you must discuss this with your local paediatric endocrinologist or named paediatrician.

Level 1: Conditions with a low level of anticipated need for input from a paediatrician with an interest in endocrinology - managed in most cases by local general paediatricians.

Level 2: Conditions with a need for input from a paediatrician with an interest in endocrinology usually managed at local DGH clinics with occasional input from a paediatric endocrinologist at regional level on a shared care basis with the local teams. For some conditions the initial diagnostic investigations may need to be undertaken at the lead centre.

Level 3: Conditions which require all or some management from a paediatric endocrinologist at regional level. These conditions are managed solely by a regional unit or through a network of endocrine clinics at the DGH, performed in combination by a regional paediatric endocrinologist and a local paediatrician with an interest in endocrinology. Some conditions that require Multi-disciplinary team (MDT) input from a number of specialists through joint clinics at regional or supra-regional level will require attendance at specialist centres for some of their visits.
DYNAMIC FUNCTION TESTS
1. GLUCOSE TOLERANCE TEST

Indications

The 2 hour standard oral glucose tolerance test may be used to:

- **Establish a diagnosis of Diabetes Mellitus.**
  
  It is unnecessary if a child has symptoms of diabetes and either a random venous plasma laboratory glucose concentration of 11.1 mmol/L or higher, or a fasting concentration of 7.0 mmol/L or higher. [Definition, Diagnosis and Classification of Diabetes Mellitus. WHO criteria 1999]. Glucose is measured at 0 min and 120 min only.

- **Assess Insulin Resistance if indicated** (see insulin resistance section below)
  
  In addition to the standard procedure glucose and insulin are measured at 0, 30, 60, 90 and 120 min.

Preparation

1. Do not perform glucose tolerance tests on patients known to be suffering from an infection, patients with uncontrolled thyroid dysfunction, or patients recovering from stress (e.g. surgery) as these alter insulin sensitivity.

2. Ensure that the child has had an adequate diet (minimum of 150g/day of carbohydrate) for at least 5 days before the test. Fast the patient overnight (4 hours for infants) but avoid more prolonged fasting. Drinks of water (no sweet drinks) are allowed during this period.

3. Calculate amount of glucose to be given
   
   a) Glucose monohydrate 1.925 g/kg (not to exceed 82.5 g - equivalent to 75g anhydrous glucose, the standard adult dose). Dissolve the dose in 100-200 mls chilled water.
   
   b) Standard Original High Glucose Drink e.g. Lucozade (45g glucose/m² max dose 75g – (1g glucose per 5.5mls original Lucozade)).

Procedure

<table>
<thead>
<tr>
<th>Time</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 min (~9 AM)</td>
<td>INSERT a reliable cannula</td>
</tr>
<tr>
<td></td>
<td>TAKE venous blood sample for laboratory glucose (and insulin if indicated).</td>
</tr>
<tr>
<td>0 min</td>
<td>GIVE Glucose drink. The drink should be fully consumed in 5-10 minutes.</td>
</tr>
<tr>
<td>120 min</td>
<td>TAKE Venous blood for lab glucose</td>
</tr>
</tbody>
</table>

(If test is being carried out to investigate Insulin Resistance collect venous blood samples at 0, 30, 60, 90 and 120 min for glucose + insulin)

Interpretation
[Diagnosis and Classification of Diabetes Mellitus. WHO criteria 1999; Expert Committee on the Diagnosis and Classification of Diabetes Mellitus 2003]

- Normal fasting plasma glucose is <5.6 mmol/L
- Normal glucose tolerance is defined by a 2 hour plasma glucose <7.8 mmol/L

**Diabetes**

Should be diagnosed only when the 2 hour plasma glucose is 11.1 mmol/L or higher. In patients without symptoms diagnosis should not be based on a single glucose determination. At least one additional glucose test result with a value in the diabetic range is required, either fasting, random or 2 hours after a standard glucose load.

- Impaired glucose tolerance
  - Is defined by a fasting plasma glucose <7.0 mmol/L and a 2 hour glucose between 7.8 and 11.1 mmol/L.

- Impaired fasting glycaemia
  - Is defined by a fasting plasma glucose between 5.6 and 7.0 mmol/L and a 2 hour concentration <7.8 mmol/L.

**Insulin resistance**

According to the recent consensus statement there is no clear cut offs to define insulin resistance in children and surrogate measures such as fasting insulin are not ideal.


Based on current screening criteria and methodology, there is no justification for screening children for insulin resistance related to obesity

We recommend, in normal individuals,

- Fasting insulin is <10 mU/L in children younger than 10 years
  - or <20 mU/L in children older than 10 years.

- Peak insulin during the test is normally <100 mU/L.

- Fasting insulin of 20 - 50 mU/L or peak insulin of 100 - 300 mU/L is suggestive of mild to moderate insulin resistance.

- Fasting insulin of >50 mU/L or peak insulin of >300 mU/L is suggestive of severe insulin resistance.
2. LUTEINISING HORMONE RELEASING HORMONE (LHRH) TEST

Indications

LHRH is an oligopeptide hormone secreted by the hypothalamus, which controls the release of luteinising hormone (LH) and follicle stimulating hormone (FSH) by the anterior pituitary gland. In older children and adults, loss of the LH and FSH response to LHRH may be an early indication of anterior pituitary disease. The LHRH test described here assesses the level of LH/FSH pituitary reserve. It may be used to investigate pubertal disorders including precocious puberty, premature breast development in girls (thelarche) and delayed puberty.

This test may be combined with Growth Stimulation tests; increase volumes of blood collected accordingly. Avoid HCG injections during the test, as cross-reaction in LH analyses gives falsely elevated results.

Preparation

There is no need to fast and the time of commencing the test is not important, unless combined with the insulin hypoglycaemia test. Insert cannula 30 min before test.

Procedure

<table>
<thead>
<tr>
<th>Time</th>
<th>Action</th>
</tr>
</thead>
</table>
| 1 0 min | INSERT a reliable cannula  
TAKE Baseline blood for LH, FSH, Oestradiol (females), Testosterone (males) |
| 2 0 min | GIVE Dose of LHRH (GnRH, gonadorelin) 100 micrograms IV over 2 min regardless of weight and age |
| 3 20 min | TAKE Blood for LH, FSH |
| 4 60 min | TAKE Blood for LH, FSH |

Interpretation

The LHRH test is often difficult to interpret and results should be interpreted alongside clinical findings; including full pubertal staging, testicular volume (boys) or ovarian ultrasound (girls). Puberty is a continuum and so is the response to the GnRH test.

Prepubertal responses: LH peak <5 U/L (LH increment less than 3-4 U/L above basal). FSH peak greater than LH (FSH increment less than 2-3 U/L above basal).

Peripubertal and pubertal responses: higher increments, especially if LH dominant, provide evidence of a pubertal pattern of gonadotrophin response: LH peak >5 U/L, with LH peak greater than FSH peak.

Pubertal Delay and Pubertal failure: In children with suspected hypogonadotrophic hypogonadism (HH), a complete lack of response supports the diagnosis. However, a measurable but low response (in the prepubertal range) may occur both in HH and in
constitutional delay of puberty and has limited predictive value. In primary gonadal failure, basal LH and FSH are elevated and their response to GnRH is exaggerated.

Precocious puberty: In gonadotrophin-independent precocious puberty spontaneous gonadotrophin secretion is suppressed by the autonomous sex steroid secretion, basal LH/FSH is low and response to LHRH is flat.

In gonadotrophin-dependent precocious puberty basal LH/FSH levels are usually (but not always) elevated and the response to LHRH is exaggerated.

Precocious puberty (treated): Suppressed basal LH/FSH and flat response to LHRH indicate adequate treatment with LHRH analogues.

Premature thelarche and thelarche variant: LH response is usually in the prepubertal range and there is a FSH predominant response.
3. HUMAN CHORIONIC GONADOTROPHIN (HCG) STIMULATION TEST

(From the Scottish DSD Network)

Introduction

Any child with an external masculinisation score (EMS, refer Figure 1) of below 11 requires further evaluation of the gonadal axis. HCG stimulation of the testes may not be necessary in early infancy and prolonged hCG test stimulation is usually not necessary in infancy. For investigation of gonadal function, the standard hCG stimulation test performed over week 1 is sufficient in many cases but some cases may require prolonged hCG stimulation. The prolonged hCG stimulation test may be a useful means of investigating the endocrine gonadal axis after infancy when the testes are nascent. They may also aid the descent of the undescended testes which are not completely impalpable. The timing of the tests is important and the results may be influenced by age and the test may influence surgical and medical management. If both gonads have never been palpable or detected, a karyotype result should be sought before embarking on the following investigative protocol, particularly in the apparent boy with premature virilisation.

Record all investigations performed.

Figure 1
**Procedure**

See table below:

<table>
<thead>
<tr>
<th>WEEK</th>
<th>Wk1</th>
<th>Wk2</th>
<th>Wk3</th>
<th>Wk4</th>
<th>&gt;Wk8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Day</strong></td>
<td>Mon</td>
<td>Tue</td>
<td>Wed</td>
<td>Thu</td>
<td>Mon</td>
</tr>
</tbody>
</table>

**COLLECT:**

<table>
<thead>
<tr>
<th></th>
<th>Wk1</th>
<th>Wk2</th>
<th>Wk3</th>
<th>Wk4</th>
<th>&gt;Wk8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Testosterone, SHBG</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Serum Androstenedione, DHT, DHEAS</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Serum AMH</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine Steroid Profile</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LHRH Stim Test (0,20,60min)</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Karyotype &amp; DNA</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**GIVE:**

<table>
<thead>
<tr>
<th></th>
<th>Wk1</th>
<th>Wk2</th>
<th>Wk3</th>
<th>Wk4</th>
<th>&gt;Wk8</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCG 1500 IM</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

**EXAMINE:**

<table>
<thead>
<tr>
<th></th>
<th>Wk1</th>
<th>Wk2</th>
<th>Wk3</th>
<th>Wk4</th>
<th>&gt;Wk8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound scan of Testes &amp; Renal Tracts</td>
<td></td>
<td></td>
<td></td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Stretched Penile length</td>
<td>*</td>
<td></td>
<td></td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Examine for Testes (Scrotal, Ing, Abdo, Absent)</td>
<td>*</td>
<td></td>
<td></td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Endocrine Follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
</tbody>
</table>

*Table 1*
1 Serum for Testosterone is very important; SHBG is much less important, particularly in infants
2 These androgens are listed in order of priority with Androstenedione being most important
3 These samples should preferably be collected on the first day but can be collected on any visit
4 All children with a DSD should have an ultrasound scan of the renal tracts

Follow-Up

Arrange endocrine clinic follow-up for 6 weeks after end of investigations.

Some children with poor testosterone response to hCG may require further assessment of adrenal function.
4. GROWTH HORMONE STIMULATION TESTS

Indication

Assessment of growth hormone deficiency

These tests are often combined with the LHRH test; the volume of blood collected will need to be increased accordingly.

The ITT (Insulin Tolerance Test)

The insulin hypoglycaemia test (also known as the insulin tolerance test, ITT) is recognised as the “gold standard” for assessment of growth hormone deficiency, particularly as it also tests the hypothalamo-pituitary-adrenal axis. This is a potentially high risk test and should only be carried out in a specialist centre where the test is being performed on a regular basis by experienced staff.

The Arginine Test for Growth Hormone

Where the ITT is not recommended or not suitable the first line test should be the Arginine test.

Clonidine test for Growth Hormone

The clonidine test is also an acceptable test for growth hormone.

Other Tests:

The Glucagon test and Exercise test for assessment of growth hormone deficiency are not recommended, due to problems with late hypoglycaemia and poor reproducibility of results, respectively.

‘Priming’ before the test

If the test is to be done on peri-pubertal children (bone age greater than 10 years, no signs of puberty in girls or testicular volume less than 8mL in boys), discuss with local paediatric endocrinologist the advisability of “priming” with the appropriate sex steroid.
4.1 INSULIN TOLERANCE TEST

Indications

Any form of stress results in secretion of the hypothalamic hormones, growth hormone releasing hormone (GHRH) and corticotrophin releasing hormone (CRH). These in turn stimulate the release of pituitary growth hormone (GH) and adrenocorticotrophic hormone (ACTH), in the latter case leading to adrenal cortisol secretion. Insulin administration is used to produce stress in the form of hypoglycaemia, and hypothalamic - pituitary - adrenal function is assessed by GH and cortisol responses to the hypoglycaemic stimulus.

This test is designed to produce symptomatic hypoglycaemia (palor, sweating). If symptoms are more severe (impaired or loss of consciousness) the child must be treated immediately (see below). Continuous observation for the symptoms of severe hypoglycaemia is essential throughout the test, and for half an hour after its completion.

Contraindications

No child with a history of epilepsy or cardiac arrhythmias should undergo this test.

Please use with caution in young children, as symptoms of hypoglycaemia may be difficult to detect.

Preparation

- The patient should be fasted overnight (4 hours for infants); drinks of water are allowed.
- Before beginning the test, have available glucose drink: 4 heaped teaspoons (equivalent to approximately 40g) dextrose powder dissolved in approximately half a glass of squash. Alternatively standard glucose drink e.g. Lucozade 50mls.
- Ensure that glucose, and hydrocortisone are also available for intravenous injection, if necessary (see emergency treatment of severe hypoglycaemia, below).
- Observe the child continuously during the test for symptoms of severe hypoglycaemia, and check the glucose concentration in each blood sample collected using the ward blood glucose meter or more frequently if the child is developing hypoglycaemic symptoms.
- If symptoms of severe hypoglycaemia do develop they must be treated immediately. See below.
- Before beginning the test, weigh the patient and insert a cannula at least 30 minutes before taking the baseline samples. The patient should be resting throughout the test. Start the test between 0800h and 0900h.
Emergency treatment of severe hypoglycaemia during the ITT

If the child does not tolerate oral glucose, or shows signs of severe hypoglycaemia (reduced conscious level) give iv treatment by giving intravenous glucose 200 mg per kg body weight (10% dextrose, 2mL per kg) over 3 minutes.

If the response is poor, give 100 mg hydrocortisone by intravenous injection. Continue with a glucose infusion iv at 10 mg per kg per minute (6 millilitres per kilogram per hour of 10% dextrose).

Check blood glucose using the ward meter after 5 min and adjust the glucose infusion to maintain a blood glucose of 5-8 mmol/L and no higher. If there is no improvement in conscious level after normal blood glucose is restored, an alternative explanation should be sought.
It is not necessary to discontinue the test and, if possible, continue blood sampling.

**IMPORTANT**
50% dextrose should NEVER be used in the resuscitation of a child with severe hypoglycaemia following an endocrine test.
### Procedure

<table>
<thead>
<tr>
<th>TIME</th>
<th>ACTION</th>
</tr>
</thead>
</table>
| 1 -30 min | INSERT a reliable cannula  
TAKE Blood for glucose, cortisol and GH determinations. (+ ward meter glucose) |
| 2 0 min | TAKE baseline blood sample for glucose, cortisol and GH. (+ ward meter glucose) |
| 3 | If blood glucose, measured using the ward meter, is less than 3.5 mmol/L in either of the two baseline samples, do NOT give insulin but continue to take blood samples (see below) and record whether child has symptoms (pale, sweating).  
If blood glucose, measured using the ward meter, is between 3.5 and 4.5 mmol/L in either of the two baseline samples, give half the dose of insulin (see below) and continue the test. |
| 4 0 min | GIVE IV soluble insulin (Actrapid) diluted with normal saline to give a solution containing 1 unit per ml.  
Dose = 0.1 units per kg body weight  
(Reduced to 0.05 units per kg in patients who might be unduly sensitive to insulin. These include patients with suspected hypofunction, those with severe malnutrition (e.g. due to anorexia nervosa) or those with baseline blood glucose between 3.5 and 4.5 mmol/L) |
| 5 | When adequate hypoglycaemia has been established (< 2.2 mmol/L laboratory blood glucose or a 50% reduction in the baseline level), or if the child shows signs of hypoglycaemia (e.g. is sweaty and drowsy), a glucose drink should be given - see preparation notes above. If this is not tolerated, or if there are more severe symptoms of hypoglycaemia (impaired or loss of consciousness), intravenous glucose may be required – see above.  
**NOTE** ward meters frequently overestimate blood glucose levels. |
| 6 15 min | TAKE blood samples for glucose, cortisol and GH (+ ward meter glucose) |
| 7 30 min | TAKE blood samples for glucose, cortisol and GH (+ ward meter glucose) |
| 8 60 min | TAKE blood samples for glucose, cortisol and GH (+ ward meter glucose) |
| 9 90 min | TAKE blood samples for glucose, cortisol and GH (+ ward meter glucose) |

### After the test

Give a sweet drink and a meal after the test and ensure that the meal has been eaten. Keep the child under observation for at least 1 hour after the meal has been consumed. Keep the cannula in position until lunch has been assimilated. Ensure that a blood glucose measured on the ward meter reads greater than 4 mmol/L before discharge. If there is any doubt about the child's wellbeing, keep him/her in overnight for observation.
**Interpretation**

If Growth Hormone >5ug/l at any point this indicates there is a normal response, which rules out growth hormone deficiency.

If Growth Hormone <5ug/l in the presence of adequate hypoglycaemia (<2.2mmol/l or 50% drop in plasma glucose < 5ug/L indicates a growth hormone deficiency.

Hypoglycaemia of this magnitude should also cause an increase in the plasma cortisol. Please check with local labs for cut offs.
4.2 ARGinine Stimulation TEST FOR GROWTH hormone

Indications

Short stature and/or consistent abnormally low growth velocity.
Growth hormone deficiency

Preparation

Patient to have water only for 8 hours prior to the test.
Arginine may cause nausea and some irritation at the infusion site.

Procedure

<table>
<thead>
<tr>
<th>TIME</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 -30 MINS</td>
<td>INSERT a reliable cannula, TAKE blood for growth hormone – baseline test.</td>
</tr>
<tr>
<td>2 -30 MINS</td>
<td>INFUSE arginine monohydrochloride IV over half an hour in a dose of 0.5g/kg up to a maximum of 30g (discuss with local pharmacist)</td>
</tr>
<tr>
<td>3 0 MINS</td>
<td>STOP infusion</td>
</tr>
<tr>
<td>4 + 0 mins + 15 mins (if also LHRH) + 30 mins + 60 mins + 90 mins + 120 mins</td>
<td>TAKE samples for growth hormone and glucose (+ ward meter glucose)</td>
</tr>
</tbody>
</table>

Samples

In children with suspected hypopituitarism prolonged fasting may induce hypoglycaemia. Blood glucose should be checked by ward meter with each sample in these patients whenever a sample is taken.

Note

This test can be combined with synacthen test to assess HPA axis in addition to growth hormone deficiency

Interpretation

If the plasma GH concentration reaches 6 ug/L or more, further investigations are not indicated. If the response is below this level, then an insulin hypoglycaemia test may be necessary.
4.3 CLONIDINE TEST FOR GROWTH HORMONE

Indication

This test is used in the investigation of suspected Growth Hormone (GH) deficiency in childhood (not in adults). Clonidine is administered orally to provoke GH release.

Preparation

Fast the patient overnight (4h for infants), and measure height and weight.

Calculate surface area from appropriate tables.

Start the test by 0900h whenever possible.

Procedure

<table>
<thead>
<tr>
<th>TIME</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>-30 min</td>
<td>INSERT reliable canula</td>
</tr>
<tr>
<td>-30 min</td>
<td>TAKE blood sample for GH</td>
</tr>
<tr>
<td>0 min (~09:00)</td>
<td>TAKE blood sample for GH</td>
</tr>
<tr>
<td>0 min</td>
<td>GIVE Clonidine (150 micrograms per m² body surface area) by mouth with a small, sugar-free drink. Round up the calculated dose to the nearest 25 micrograms. (after completion)</td>
</tr>
<tr>
<td>30 min</td>
<td>TAKE blood sample for GH</td>
</tr>
<tr>
<td>60 min</td>
<td>TAKE blood sample for GH</td>
</tr>
<tr>
<td>90 min</td>
<td>TAKE blood sample for GH</td>
</tr>
<tr>
<td>120 min</td>
<td>TAKE blood sample for GH</td>
</tr>
<tr>
<td>150 min</td>
<td>TAKE blood sample for GH</td>
</tr>
</tbody>
</table>

After the test

Side effects of Clonidine (hypotension and drowsiness) may persist for several hours after the test. Keep the patient lying down for at least an hour after the test, and check pulse and blood pressure half-hourly and also before allowing him/her to get up. Careful observation of the patient is necessary until late afternoon.

Interpretation

If the plasma GH concentration reaches 6 ug/L or more, further investigations are not indicated. If the response is below this level, then an insulin hypoglycaemia test may be necessary.
5.0 STANDARD SHORT SYNACTHEN TEST

Indications

The synthetic polypeptide Synacthen (Tetracosactrin BP) has a structure identical to the N-terminal 24 amino acids of Adrenocorticotropic Hormone (ACTH). It has a short duration of action and permits a rapid and convenient screening test for the assessment of adrenocortical function by measuring cortisol response.

Measurement of additional adrenal steroids during the test (at the same time as the samples for cortisol - see below) may also be used to assess the steroid biosynthetic pathway. Plasma 17-hydroxyprogesterone (17-OHP) measurements may assist in the diagnosis of non-salt-losing congenital adrenal hyperplasia. If a defect in steroid biosynthesis is suspected, also collect a random urine specimen for a full steroid profile before the Synacthen test.

Preparation

1. Prednisolone and hydrocortisone both interfere with the measurement of cortisol. If the patient is already on hydrocortisone ask the patient to omit their doses the evening before and on the morning of the test. The patient should continue taking the hydrocortisone immediately after the test whilst waiting for results. The Synacthen test should not be performed if the patient has been on Prednisolone within the last 2 weeks.

2. The patient need not be fasting. Insert a cannula at least 30 minutes before taking the baseline sample.

Procedure

<table>
<thead>
<tr>
<th>TIME</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 0 min</td>
<td>INSERT a reliable cannula&lt;br&gt;TAKE blood for cortisol</td>
</tr>
<tr>
<td>2 0 min</td>
<td>GIVE Synacthen (tetracosactride) IV and flush in well with 0.9% saline. For children, the dose is 250 micrograms. For neonates and infants &lt;7kg, dose by weight is 36 micrograms/kg (rounded to the nearest 25 micrograms)</td>
</tr>
<tr>
<td>3 30 min</td>
<td>TAKE blood for cortisol</td>
</tr>
<tr>
<td>4 60 min</td>
<td>TAKE blood for cortisol</td>
</tr>
</tbody>
</table>

Interpretation

Cortisol responses at 60 min are usually >650 nmol/L in children <6y, or >470 nmol/L in children 6-18y.

The exact values of cortisol cutoffs will be affected by the method used. Please consult your local laboratory.
Interpretation of plasma 17-OHP depends on age and clinical presentation. Both adults and children usually have baseline 17-hydroxyprogesterone concentrations less than 6 nmol/l.

In late onset congenital adrenal hyperplasia, the baseline 17-hydroxyprogesterone may be either normal or high, but there is an exaggerated response (>30nmol/l) to Synacthen stimulation.
6.0 WATER DEPRIVATION TEST

This test is used when the diagnosis of Diabetes Insipidus (DI) is in doubt. As most cases of DI can be confirmed or excluded on history and baseline investigations, this test is generally not recommended. **This test can be potentially dangerous** and is very distressing to the patient.

We suggest patients should be discussed with the tertiary centre before consideration of the test. It maybe more appropriate for the test to be carried out in the tertiary centre.

For this reason, a protocol for the water deprivation test is not part of this handbook.

PSYCHOGENIC POLYDIPSIA: the vast majority of children who appear to be drinking too much have “psychogenic polydipsia” (habitual drinking), and are usually able to concentrate their urine appropriately. Many have become habitual juice drinkers and will reduce their intake if only water is offered.

Assess after allowing access to water, but restricting juice and other flavoured fluids. (children with DI will continue to drink large amounts).

Initially check an early morning urine for osmaolarity:
- >800 mosm/l will exclude Diabetes Insipidus
- <300 mosm/l - check an early morning fasting urine. Child should be allowed water only to drink the day before (no juice etc)

Unusual features more likely to be seen in Diabetes Insipidus:
- drinking unusual fluids such as bath water, pets water
- drinking through the night
- new onset enuresis.

If DI is still considered, please discuss with your tertiary centre.
**7.0 DEXAMETHASONE SUPPRESION TEST**

**Indications**

This test is used to identify Cushings Syndrome. Initially the The Overnight Dexamethasone Suppression Test is used to screen.

If there is a failure of suppression, a prolonged dexamethasone test may be required and this should be discussed with your local tertiary endocrinologist. In this case a The Prolonged (Low or high dose) Dexamethasone Suppression Test may help confirm Cushing’s syndrome and elucidate the cause.

**Overnight Dexamethasone Suppression Test**

**Procedure**

<table>
<thead>
<tr>
<th>TIME</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Between 2300h and midnight</td>
<td>GIVE the patient oral Dexamethasone (children 10 micrograms per kg body weight, adults 1 milligram. Dexamethasone is available as scored 500 microgram tablets - round the dose to the nearest 250 micrograms (i.e. half a tablet).</td>
</tr>
<tr>
<td>2 0900h the next day</td>
<td>Take blood for cortisol.</td>
</tr>
</tbody>
</table>

**Interpretation**

In normal subjects, the 0900h plasma cortisol is suppressed to less than 50 nmol/l. In patients with Cushing’s syndrome, such marked suppression is not observed. Patients taking hepatic enzyme-inducing drugs (e.g. phenytoin, phenobarbitone) may have false negative results.
PROLONGED TESTS

Low Dose Dexamethasone Suppression Test

Indications
Diagnosis of Cushing’s syndrome.

Precautions/Preparation
Ensure that urine is collected for 24 hour urinary free cortisol and steroid profile before the test.

Procedure

<table>
<thead>
<tr>
<th>TIME</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Day 1 0900</td>
<td>TAKE blood samples for cortisol and ACTH. COMMENCE Urine collection for 24h urinary free cortisol and steroid profile</td>
</tr>
<tr>
<td>2 Day 1 2400</td>
<td>TAKE blood for cortisol and ACTH</td>
</tr>
<tr>
<td>3 Days 2 and 3</td>
<td>GIVE oral dexamethasone 0.5mg 6 hourly (or 20 micrograms/kg/dose 6-hourly for younger children) (Total of 8 doses)</td>
</tr>
<tr>
<td>4 Day 4 0600</td>
<td>TAKE blood for cortisol and ACTH. Commence urine collection for 24h urinary free cortisol and steroid profile.</td>
</tr>
</tbody>
</table>

Interpretation
Normal: Cortisol level should suppress to <50nmol/L.

Patients with Cushing’s syndrome, from whatever cause, lose the normal negative feedback control by circulating glucocorticoids on ACTH release and thus exhibit detectable plasma ACTH and cortisol concentrations after dexamethasone administration.

In patients who fail to suppress, a pre-test ACTH level of <5ng/L is highly suggestive of an adrenal cause of Cushing’s syndrome.

High Dose Dexamethasone Suppression Test

Indications
To differentiate pituitary-dependent and ectopic causes of Cushing’s syndrome.

Precautions/Preparation - nil
Procedure

<table>
<thead>
<tr>
<th>TIME</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Day 1 0900*</td>
<td>TAKE blood samples for cortisol and ACTH. Commence Urine collection for 24h urinary free cortisol and steroid profile</td>
</tr>
<tr>
<td>2 Day 1 2400</td>
<td>TAKE blood for cortisol and ACTH</td>
</tr>
<tr>
<td>3 Days 2 and 3</td>
<td>GIVE oral dexamethasone 2mg 6 hourly (or 80 micrograms/kg/dose 6-hourly for younger children) (total of 8 doses)</td>
</tr>
<tr>
<td>4 Day 4 0600</td>
<td>TAKE blood for cortisol and ACTH. Commence Urine collection for 24h urinary free cortisol and steroid profile. Low and high dose dexamethasone suppression tests may be performed sequentially if desired, in which case start high dose at 0600 on day after low dose test is completed</td>
</tr>
</tbody>
</table>

Interpretation

Pituitary-dependent hypercortisolism (Cushing’s disease): plasma cortisol usually suppresses to at least 50% of basal values.

NB Approximately 10% of patients with Cushing’s disease fails to suppress and approximately 10% of those with ectopic ACTH secretion will suppress.
## APPENDIX 1

### Paediatric Endocrinologists

<table>
<thead>
<tr>
<th>Health Board</th>
<th>Consultant Endocrinologists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lothian</td>
<td>Dr Louise Bath, Consultant Endocrinologist</td>
</tr>
<tr>
<td>Edinburgh Royal Hospital for Sick Children</td>
<td>Dr Harriet Miles, Consultant Endocrinologist</td>
</tr>
<tr>
<td>0131 536 0000</td>
<td></td>
</tr>
<tr>
<td>Glasgow and Clyde</td>
<td>Dr Guftar Shaikh, Consultant Endocrinologist</td>
</tr>
<tr>
<td>Glasgow Royal Hospital for Sick Children</td>
<td>Professor Faisal Ahmed, Consultant Endocrinologist</td>
</tr>
<tr>
<td>0141 201 0000</td>
<td>Dr Malcolm Donaldson, Consultant Endocrinologist</td>
</tr>
<tr>
<td>Grampian</td>
<td>Dr Amalia Mayo, Consultant Paediatrician</td>
</tr>
<tr>
<td>Royal Aberdeen Children’s Hospital</td>
<td></td>
</tr>
<tr>
<td>0845 456 6000</td>
<td></td>
</tr>
<tr>
<td>Tayside</td>
<td>Dr Steve Greene, Consultant Paediatrician</td>
</tr>
<tr>
<td>Ninewells Hospital</td>
<td></td>
</tr>
<tr>
<td>01382 660111</td>
<td></td>
</tr>
</tbody>
</table>

### Paediatricians with an interest in Endocrinology

<table>
<thead>
<tr>
<th>Health Board</th>
<th>Consultant Paediatrician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dumfries and Galloway</td>
<td>Dr Raj Shyam, Consultant Paediatrician</td>
</tr>
<tr>
<td>Fife</td>
<td>Dr Ahmad Ainine, Consultant Paediatrician</td>
</tr>
<tr>
<td>Victoria Infirmary</td>
<td></td>
</tr>
<tr>
<td>Highland</td>
<td>Dr George Farmer, Consultant Paediatrician</td>
</tr>
<tr>
<td>Raigmore Hospital</td>
<td></td>
</tr>
<tr>
<td>Ayrshire and Arran</td>
<td>Dr Scott Williamson, Consultant Paediatrician</td>
</tr>
<tr>
<td>Crosshouse Hospital</td>
<td>Dr Jon Staines, Consultant Paediatrician</td>
</tr>
<tr>
<td>Forth Valley</td>
<td>Dr John Schulga, Consultant Paediatrician</td>
</tr>
<tr>
<td>Forth Valley Royal</td>
<td></td>
</tr>
<tr>
<td>Borders</td>
<td>Dr Andy Duncan, Consultant Paediatrician</td>
</tr>
<tr>
<td>Borders General Hospital</td>
<td></td>
</tr>
<tr>
<td>Lanarkshire</td>
<td>Dr Ian Hunter, Consultant Paediatrician</td>
</tr>
<tr>
<td>Wishaw General Hospital</td>
<td></td>
</tr>
</tbody>
</table>