ICE Test Name: None – Please request tests separately

This test is potentially dangerous and must be undertaken with great care. Patients unable to conserve water may rapidly become severely hypertonic during this test.

Arrangements for carrying out a Water deprivation Test:

When a decision is taken, either in clinic or on the ward, to perform a water deprivation test, to arrange for this test, please action as follows:

1. Inform Paediatric Endocrine Secretary
   - Drs Padidela / Skae x11628 Joanne Davis
   - Drs Murray / Mughal/ Chinoy x11678 Janet Hughes
   - Drs Banerjee / Clayton / Patel/ Salomon Estebanez x11632 Sue Wilkinson

2. Secretary to contact Anne Shenton on x12233, Paediatric Lead in Biochemistry, with information regarding time line for performing these tests and underlying diagnosis. (Contact the paediatric Duty Biochemist on x12255 if difficulty in getting through to Anne Shenton)
   - State if urgent or routine

3. Biochemistry provides Endocrine secretary with feasible dates.

4. Secretary to discuss with ETC for booking admission on one of the days feasible for biochemistry
   - Admission will be on Short Stay Ward from approx 4.00 pm for overnight stay for bloods/osmolality etc. as per protocol, followed by early morning admission on MIU early the following morning for Water Deprivation Test.

5. Secretary informs endocrine doctors and biochemistry about the date agreed with the ETC and the family.

Principle
Water restriction in normal individuals results in the secretion of AVP from the posterior pituitary in order to reabsorb water from the distal renal tubules and concentrate urine. Failure of this mechanism occurs in diabetes insipidus (DI), resulting in a rise in plasma osmolality, due to water loss, and a dilute urine of low osmolality. The concentrating mechanism for urine is maintained in compulsive water drinking (CWD). Cranial DI is caused by a failure of AVP secretion whilst nephrogenic DI is caused by insensitivity of the renal tubules to AVP. The two forms of DI can be distinguished by the administration of Desamino-D-AVP (DDAVP; synthetic AVP).

Indication
- This test is used to distinguish DI from primary polydipsia and to investigate suspected cranial or nephrogenic DI.
- A subjective thirst score may be performed at the same time and requires copies of the unit-less 100 mm linear visual analogue scale.

Precautions
- This test should not be performed if there is evidence of the kidney’s ability to concentrate urine e.g. spot urine osmolality >750 mmol/kg.
- Other causes of polyuria and polydipsia MUST be excluded before proceeding with the test. These include:
  - Diabetes mellitus
  - Hypoadrenalism
  - Hypercalcaemia
- Hypokalaemia
- Hypothyroidism
- Urinary infections
- Chronic kidney disease
- Therapy with carbamazepine, chlorpropamide or lithium

Cortisol insufficiency must be treated prior to doing a water deprivation test as it interferes with the ability to excrete water and can mask DI.

**Side Effects**

- Patients with true DI may become severely water depleted during this test and **MUST** be carefully monitored (by weighing the patient and quantifying urine output regularly) throughout the test.

**Preparation**

*The laboratory MUST be notified AT LEAST 24 hrs before the test, ideally with more notice. Please see instructions on previous page. Osmolality results are required as soon as possible after the specimens have been collected.*

- Before considering the test, polyuria must be established with an accurate 24 hr urine output measurement. Urine output >4 mL/kg/hr in infants and children >1 year old is suggestive of polyuria.
- *The overnight test is reserved for situations where the diagnosis cannot be easily made by stopping oral fluid intake for a few hours and obtaining sodium and osmolality measurements.*
- *Children with massive polyuria (>4L/24 hr) should start the test in the morning when medical staff are present as the test will usually last 2–4 hrs.*
- Thyroid and adrenal function must be normal or adequately replaced.
- The patient must be kept under close surveillance throughout the test to avoid surreptitious water drinking and in order to be monitored for any signs of dehydration.
- During the test the child should be allowed to eat snacks with no fluid intake of milk, juice or water. Dry snacks such as biscuits or crisps would be preferable.

**Protocol**

1. The night before the test (at 2200h), take blood for bedside glucose, plasma osmolality, urea, electrolytes, glucose and Co-peptin.
   - **The test can only be carried out if the plasma osmolality is <295 mmol/kg.**
   - Plasma osmolality can be calculated from the urea, electrolyte and glucose results using the formula:
     
     $$\text{Calculated plasma osmolality} = (2 \times \text{Na}) + \text{Glucose} + \text{Urea}$$
   - The osmolality sample will be analysed by the lab first thing in the morning before the test commences.

2. If the test is to proceed, weigh the patient undressed, record the weight and insert a reliable i.v. cannula.

3. Assess the patient:
   - If there is a low level of suspicion of DI and the patient is >2 years of age, stop all fluid intake at midnight.
   - If there is a high index of suspicion of DI (i.e. patients are polyuric or borderline hyperosmolar), or if the child is <2 years of age, fluid restriction should commence in the morning.

4. **Print out the water deprivation template on page 49 and fill in.**

5. At 0900h weigh the patient undressed and record the weight. Calculate and record 5% of the weight. Collect blood and urine samples for bedside glucose, osmolality, urea, electrolytes and Co-peptin. The samples should be sent **immediately** to the Biochemistry laboratory.
   - **If the osmolality is >295 mmol/kg the water deprivation test must not be undertaken.**

6. On hourly basis, undertake the following and record on the table below:
   a. Record fluid input and output – this must be strictly charted
   b. Collect blood for bedside glucose, urea and electrolytes and serum osmolality
   c. Collect urine sample for urine osmolality
d. Measure and record heart rate and blood pressure

e. Weigh the child and record on table. For measurement of weight, the child should be undressed or measured wearing the same clothing. Inform paediatric endocrine team if weight loss of more than 5% occurs. They will consider termination of test with administration of DDAVP.

7. The test is normally continued until 3 consecutive urines have shown a total rise in urine osmolality of <30 mmol/kg (normally about 12 midday) or until either:

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>The urine osmolality exceeds 750 mmol/kg (or 500 mmol/kg in infants)</td>
</tr>
<tr>
<td>5% of initial weight is lost or thirst is unbearable</td>
</tr>
<tr>
<td>Plasma osmolality exceeds 300 mmol/kg</td>
</tr>
</tbody>
</table>

N.B. It may be necessary to prolong the test in compulsive water drinking, especially if the child has been drinking excessively immediately prior to the start.

7. At 12 midday, or when the test is terminated, take blood samples for urea, electrolytes, osmolality and Co-peptin, along with a urine sample for osmolality.

N.B. If 5% weight loss or extreme distress occurs, give DDAVP (5 micrograms intra-nasally or 0.3 microgram i.m.) and free fluids immediately after test is terminated.

8. If the child shows no evidence of urinary concentration, proceed with the DDAVP test to allow differentiation between central and nephrogenic DI.

9. It is unlikely that child has DI if the child fails to pass urine during the duration of water deprivation test and clinically remains well.

DDAVP Test

1. Allow the patient to drink but not excessively or a dilutional hyponatraemia may occur.

N.B. Fluid intake should be no more than twice the volume of urine passed during fluid restriction. Fluid intake should be monitored closely.

2. Give subcutaneous or intranasal DDAVP as follows (*Desmopressin treatment must be discussed with the on-call endocrinologist*):

**Dose of Subcutaneous Desmopressin**

- 0 – 2 years 0.04 micrograms/kg maximum initial dose 0.4 micrograms
- 2 – 12 years 0.4 - 1 microgram
- >12 years – 0.7 - 1 microgram

**Dose of intra-nasal desmopressin**

- Children aged 12 – 18 years or 20 micrograms intra-nasally
- Children aged 2 to 12 years 10 – 20 micrograms intra-nasally

2. Collect blood and urine samples for osmolality hourly (if possible) for the next 4 hours. If necessary this can continue to 6 hours to obtain a diagnostic result allowing hourly blood glucose monitoring and allowing the child to eat dry food. Stop the test if the urine osmolality reaches >750 mmol/kg.

**Samples**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sample Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na, K, Urea &amp; Plasma Osmolality</td>
<td>1 mL lithium heparin blood (orange top)</td>
</tr>
<tr>
<td>Glucose</td>
<td>1 mL venous blood in a fluoride oxalate tube (yellow top)</td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>1-2 mL urine in a plain bottle</td>
</tr>
<tr>
<td>Co-peptin</td>
<td>1 mL lithium heparin (orange top). The laboratory will only send co-peptin for analysis if the urine and plasma osmolality results are indicative of Diabetes Insipidus.</td>
</tr>
</tbody>
</table>

**Interpretation**

Normal and CWD: Plasma osmolality does not exceed 295 mmol/kg and the urine osmolality rises three-fold to >750 mmol/kg.
Central DI: Plasma osmolality >295 mmol/kg with inappropriately dilute urine (<300 mmol/kg). DDAVP produces normally concentrated urine.

Nephrogenic DI: As for Central DI, but DDAVP produces no response.

Partial DI: Patients have moderate elevation of plasma osmolality and urine osmolality typically between 300-750 mmol/kg.

Copeptin: There are currently no reference ranges for Co-peptin in children. The following ranges are derived from limited studies in adult populations:

- Baseline Co-peptin levels (without prior thirsting):
  - ≥21.4 pmol/L – Suggests nephrogenic DI
  - <21.4 pmol/L – Suggests other polyuria-polydipsia syndromes (including cranial DI)
  - <2.6 pmol/L – Suggests cranial DI

- Stimulated Co-peptin levels (plasma osmolality >300 mmol/kg):
  - <4.9 pmol/L – Suggests cranial DI
  - >6.5 pmol/L - Suggests primary polydipsia

Plasma-urine osmolality relationship in adults and children adapted from Harrison's principles of internal medicine 1998.2
Plasma urine osmolality relationships in full term and pre-term infant graphs are taken from Great Ormond street protocol book.
**Water deprivation test template**

Date:_____________________

Name_________________________  Date of Birth:__________  Hospital Number:_____________________

The night before the test (at 2200h), take blood for bedside glucose, plasma osmolality, urea, electrolytes, glucose and Co-peptin.

Fluids restricted since (if overnight fluid restricted):

Water deprivation test started at (ideally 9 am):

<table>
<thead>
<tr>
<th>Patient weight</th>
<th>Kg</th>
<th>Calculate weight minus 5 %</th>
<th>Kg</th>
</tr>
</thead>
</table>

Test must be stopped if weight loss exceeds 5 %.
Test must be stopped if serum osmolality exceeds 300 mOsm/kg

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>Weight</th>
<th>Bedside Blood Glucose</th>
<th>HR</th>
<th>BP</th>
<th>Serum osmolality</th>
<th>Urine Osmolality</th>
<th>Urine output</th>
</tr>
</thead>
</table>

Please note - the test should only be stopped after discussion with the named consultant.

The test is normally continued until:

- 3 consecutive urines have shown a total rise in urine osmolality of <30 mmol/kg (normally about 12 midday)
- The urine osmolality exceeds 750 mmol/kg (or 500 mmol/kg in infants)
- 5% of initial weight is lost or thirst is unbearable
- Plasma osmolality exceeds 300 mmol/kg
Endocrine Dynamic Function Test Protocols for use in Neonates and Children

References