Water Deprivation Test

Test Name: CHILD WATER DEPRIVATION TEST

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.

2. Secretary to discuss with dates for admission with ETC.

    - 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.

3. Secretary contacts Duty Biochemist on extension 12255 to check if date suitable.

4. Duty Biochemist adds test to lab diary (for day after admission)

5. Secretary confirms date with ETC.

Principle

Water restriction in normal individuals results in the secretion of arginine vasopressin (AVP) from the posterior pituitary in order to reabsorb water from the distal renal tubules and concentrate urine. Failure of this mechanism results 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). AVP-deficiency (formerly known as cranial diabetes insipidus) is caused by a failure of AVP secretion whilst AVP-resistance (formerly known as nephrogenic diabetes insipidus) is caused by insensitivity of the renal tubules to AVP. The two AVP disorders can be distinguished by the administration of desmopressin (synthetic AVP).

Indication

- This test is used to distinguish AVP disorders from primary polydipsia and to identify whether AVP deficiency or resistance is present.
- 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 an AVP disorder.

Side Effects

- Patients with AVP deficiency/ resistance 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 copeptin.
   - *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:*

     Calculated plasma osmolality = (2 x Na) + Glucose + 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 an AVP disorder and the patient is >2 years of age, stop all fluid intake at midnight.
   - If there is a high index of suspicion of an AVP disorder (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 copeptin. 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, plasma urea and electrolytes, plasma osmolality and plasma copeptin.**
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 desmopressin.**

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:

- 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.

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 copeptin, along with a urine sample for osmolality.
N.B. If 5 % weight loss or extreme distress occurs, give desmopressin (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 desmopressin test to allow differentiation between AVP-deficiency and AVP-resistance.

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

Desmopressin Test

Test Name: CHILD WATER DEPRIVATION TEST DDAVP EXTENSION

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 desmopressin as follows ***(Desmopressin treatment must be discussed with the on-call endocrinologist):***

Age	*Generic*	*Route*	*Dose*	*Frequency*
0-2 years	*Desmopressin*	*Subcutaneous*	*0.04 micrograms/kg maximum initial dose 0.4 micrograms*	*Bolus*
2-12 years	*Desmopressin*	*Subcutaneous*	*0.4 - 1 microgram*	*Bolus*
2-12 years	*Desmopressin*	*Intranasal*	*10 – 20 micrograms*	*Bolus*
>12 years	*Desmopressin*	*Subcutaneous*	*0.7 - 1 microgram*	*Bolus*
12-18 years	*Desmopressin*	*Intra-nasal*	*20 micrograms*	*Bolus*

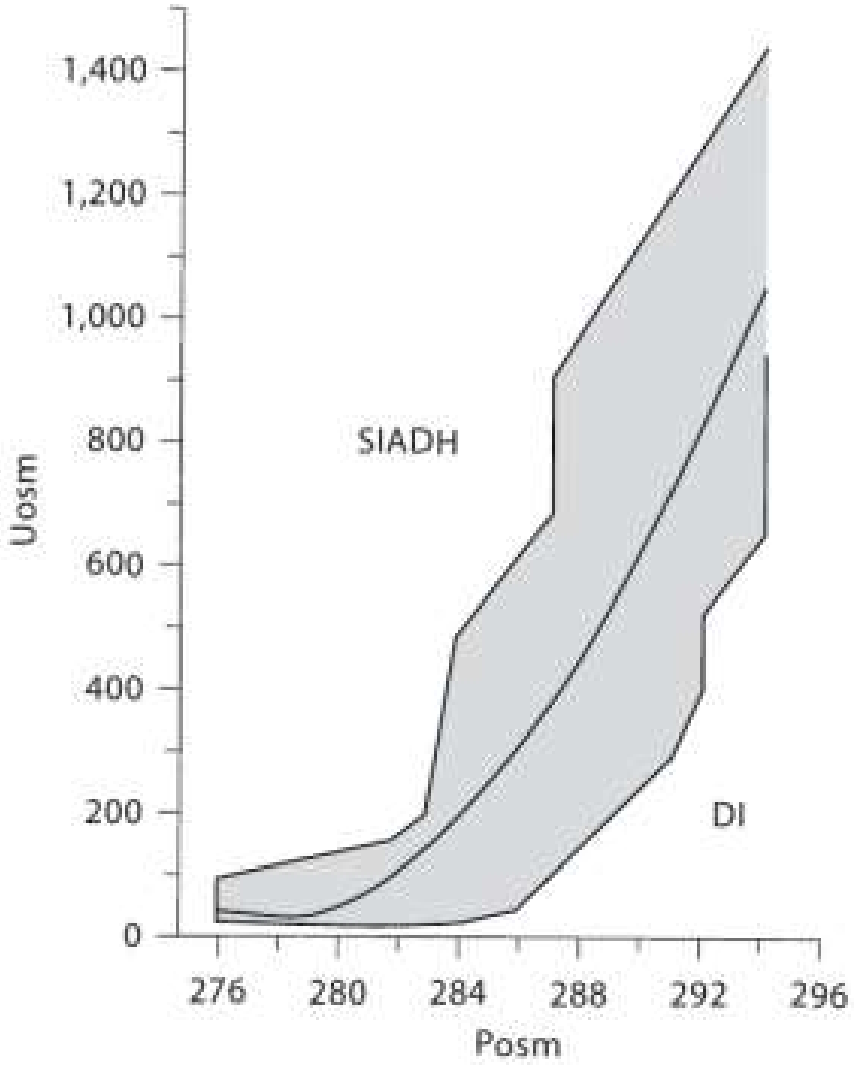
3. Collect blood and urine samples for osmolality hourly (if possible) for the next 4 hours. If necessary, this can continue to 6 hours to obtain a diagnostic result allowing hourly blood glucose monitoring and allowing the child to eat dry food. Stop the test if the urine osmolality reaches >750 mmol/kg.

Samples

Na, K, Urea & Plasma Osmolality	1.2 mL lithium heparin blood (orange top)
Glucose	1.2 mL fluoride oxalate tube (yellow top)
Urine osmolality	1-2 mL urine in a plain bottle
Copeptin	1.2 ml lithium heparin (orange top). The laboratory will only send copeptin for analysis if the urine and plasma osmolality results are indicative of an AVP disorder. The sample collected at the time of the highest osmolality will be sent.

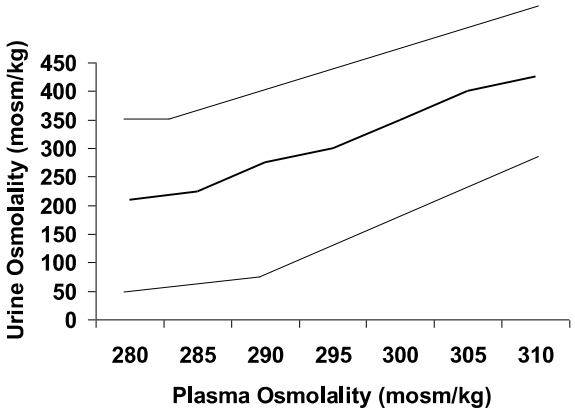
Interpretation

Normal and CWD:	Plasma osmolality does not exceed 295 mmol/kg and the urine osmolality rises three-fold to >750 mmol/kg.
AVP-deficiency:	Plasma osmolality >295 mmol/kg with inappropriately dilute urine (<300 mmol/kg). Desmopressin produces normally concentrated urine.
AVP-resistance:	As for Central DI, but desmopressin produces no response.
Partial AVP disorder:	Patients have moderate elevation of plasma osmolality and urine osmolality typically between 300-750 mmol/kg.
Copeptin:	There are currently no reference ranges for copeptin in children. The following ranges are derived from limited studies in adult populations: <u>Baseline copeptin levels (without prior thirsting):</u> ≥21.4 pmol/L – Suggests AVP-resistance. <21.4 pmol/L – Suggests other polyuria-polydipsia syndromes (including AVP-deficiency) >5 pmol/L – Suggests that AVP-deficiency is unlikely (even with a normal serum sodium/osmolality) <2.6 pmol/L – Suggests AVP-deficiency. <u>Stimulated copeptin levels (plasma osmolality >300 mmol/kg):</u> <4.9 pmol/L – Suggests AVP-deficiency >6.5 pmol/L - Suggests primary polydipsia

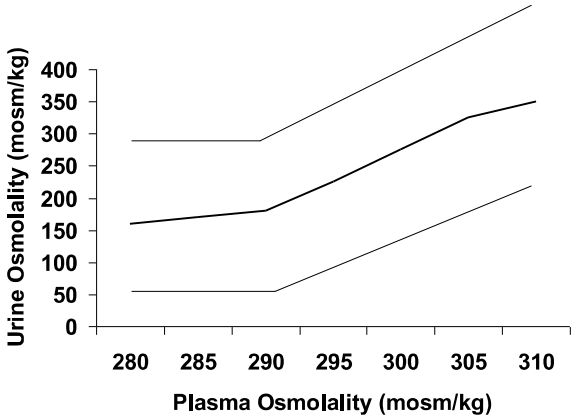


Plasma-urine osmolality relationship in adults and children adapted from Harrison's principles of internal medicine 1998[2].

PLASMA-URINE OSMOLALITY RELATIONSHIP IN FULLTERM NEWBORNS



PLASMA-URINE OSMOLALITY RELATIONSHIP IN PRETERM INFANTS



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 copeptin.

Fluids restricted since (if overnight fluid restricted):

Water deprivation test started at (ideally 9 am):

Patient weight	Kg	Calculate weight minus 5 %	Kg

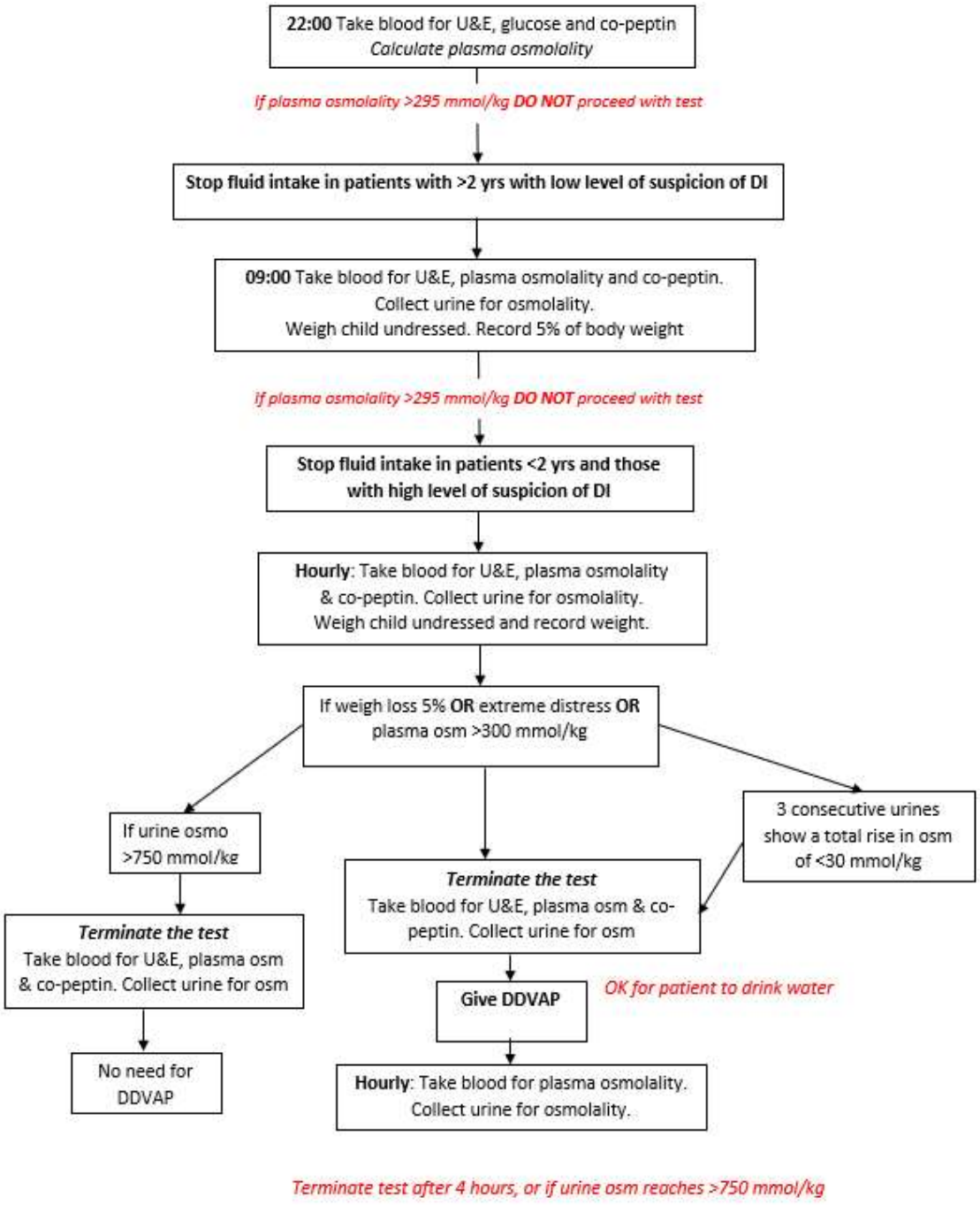
Test must be stopped if weight loss exceeds 5 %.
Test must be stopped if serum osmolality exceeds 300 mOsm/kg

Date/Time	Weight	Bedside Blood Glucose	HR	BP	Serum osmolality	Urine Osmolality	Urine output

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.



References

1. Di Iorgi N., Napoli F., Allegri A.E.M., Olivieri I., Bertelli E., Gallizia A., Rossi A. & Maghnie M. (2012) Diabetes Insipidus – Diagnosis and management. *Horm Res Paediatr* **77**: 69 – 84
2. Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2000
3. Harrison's principles of internal medicine 14th Edition 1998.