East Kent Hospitals University NHS Foundation Trust

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POLYURIA: GUIDELINES FOR INVESTIGATION

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Director responsible for implementation:	Dr. Edmund Lamb (Clinical Director)
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Target audience:	Clinical staff (medical, nursing and scientific), Trust wide and primary care

We care

Version Control Schedule

Version	Date	Author	Status	Comment
	Sep 2015	Dr. Edmund Lamb	Archive	Archived following review – This document has replaced BIO NO 022 (WATER DEPRIVATION TEST: INVESTIGATION OF SUSPECTED DIABETES INSIPIDUS (DI))
1.0	Nov 2020	Dr. Edmund Lamb/ Gifty George	Archive	Archived
2.0	Aug 2022	Dr. Edmund Lamb/ Gifty George	Active	Reference to arginine stimulation test. Updated to the new format.

Consultation and Ratification Schedule

Name and Title of Individual	Date Consulted
Dr S Joseph, Consultant Endocrinologist	January 2021

Name of Committee	Date Reviewed
PMGC and CSS governance meeting	October 2022

Contents

1. Introduction, Background and Purpose

Polyuria is defined as production of large volumes of urine (>3 L/day in adults and 2 L/m^2 in children). A thorough clinical history is essential to differentiate polyuria from the common complaints of frequency or nocturia, which may not be associated with an increase in the total urine output.

Polyuria may be caused by an osmotic diuresis (hypertonic polyuria), such as hyperglycaemia, or a water diuresis (hypotonic polyuria), such as diabetes insipidus.

2. Definitions

- **Polyuria**: urine output exceeding 3 L/day in adults and 2 L/m^2 in children
- **Primary polydipsia**: excessive intake of fluids
- **Antidiuretic hormone (ADH)**: hormone released by the posterior pituitary to regulate extracellular fluid volume by regulating the volume and osmolality of the urine
- **Arginovasopressin (AVP):** alternative name for ADH
- **Desmopressin (DDAVP):** synthetic analogue of ADH
- **Diabetes insipidus (DI):** disorder characterised by excretion of large volumes (>3 L/day) of dilute urine (<300 mOsm/kg)
- **Hypertonic polyuria:** urine with an osmolality of >750 mOsm/kg
- **Hypotonic polyuria:** urine with an osmolality of <300 mOsm/kg
- **Cranial diabetes insipidus (CDI)**: disease in which large volumes of dilute urine (polyuria) are excreted due to ADH deficiency
- **Nephrogenic diabetes insipidus (NDI)**: disease in which large volumes of dilute urine (polyuria) are excreted due to ADH resistance

3. Scope

This guideline outlines the biochemical investigation required to investigate the different causes of polyuria and the further investigation of diabetes insipidus. It may be used for patients both within EKHUFT and in primary care and the community.

4. Guidance

4.1 Investigations

Initial investigations should include collecting a 24 hr urine sample and requesting 24 hr urine creatinine to confirm that the patient is polyuric (>3 L/day). If polyuria is confirmed, the next investigation should include measurement of urine osmolality. To determine if able to concentrate urine, the patient should collect an early morning urine sample, following water restriction overnight, i.e. from going to bed, as long as that is safe to do so (i.e. the patient does not become uncomfortably thirsty, or it is a heat wave). A paired serum sample should also be collected for measurement of serum osmolality and sodium. In the presence of polyuria, urine osmolality ≥750 mOsm/kg (hypertonic) with normal serum sodium concentration excludes diabetes insipidus.

Other causes of polyuria include:

- **Diabetes Mellitus**
  Fasting glucose and/or HbA1c should be requested if diabetes is suspected, particularly if the patient has an associated history of weight loss (type 1 diabetes) or a family history of diabetes (type 2 diabetes).
- **Kidney disease**
  Measurement of serum creatinine and estimation of GFR. Severe chronic kidney disease can occasionally give rise to either polyuria or nocturia.
- **Urinary tract infection**
  Urine reagent strip to look for presence of leucocytes or nitrites.
- **Hypercalcaemia**
- **Hypokalaemia**
- **Drugs –** carbamazepine, lithium or mannitol therapy

If urine osmolality is <750 mOsm/kg and the patient is polyuric, then diabetes insipidus (DI) cannot be excluded.

Diabetes insipidus (DI) is a disorder where the body is unable to conserve water, resulting in a rise in plasma osmolality, profound polyuria and polydipsia. There are two forms of DI: cranial diabetes insipidus (CDI) occurs due to the lack of arginine vasopressin (AVP) hormone (also known as antidiuretic hormone, ADH), released from the posterior pituitary,

whereas nephrogenic diabetes insipidus (NDI) occurs due to a defect in the kidney's response to AVP. Besides polyuria and polydipsia, other clinical signs and symptoms may include nocturia, dilute urine and hypotension. In contrast, primary polydipsia is a disorder where an individual consumes large volumes of fluid producing large volumes of dilute urine. This is often a psychological disorder and has been associated with drugs causing oral dryness.

The water deprivation test is used in the differential diagnosis of polyuria, separating CDI, NDI and primary polydipsia.

For patients for whom a water deprivation test is contra-indicated, an arginine stimulation test may be considered. However, patients must be referred to an Endocrinologist and the test is performed in the Medical Day Unit at K&CH. Arginine-stimulated copeptin measurement protocol can be found on Q-pulse (BIO-EX-611).

4.2 Water deprivation test

Principle

The principle of this test is to assess if the patient can concentrate urine when deprived of fluids. Water deprivation should normally cause increased AVP secretion, resulting in the production of concentrated urine. In addition, serum osmolality measurements can assist with indicating the type of the underlying polyuric state, as high plasma osmolality (≥295 mOsm/kg) is typically seen in DI while a normal or low plasma osmolality (<295 mOsm/kg) is usually seen in primary polydipsia.

This test cannot be performed in primary care. It should only be undertaken after discussion with a consultant nephrologist or endocrinologist. In paediatrics, the test should only be performed at a tertiary referral centre after discussion with a visiting consultant paediatrician.

Patient preparation

DDAVP and diuretics such as furosemide and bendroflumethiazide should be stopped 24 hr before the test. Smoking, alcohol, tea and coffee are forbidden to the patient throughout the whole procedure, as they can directly stimulate the secretion of AVP independently of the osmoreceptors. Before performing a water deprivation test, please request cortisol (sample collected at 9 am) and thyroid function tests (TFTs), as hypoadrenalism and hypothyroidism may impair excretion of a free water load, and must be treated prior to proceeding.

The test

Always contact the laboratory before starting the test to ensure that rapid analysis of urine and serum samples will be available. A template is provided to record the patient's weight and osmolality at different time-points (Appendix A). The patient must be kept under observation for the entire period of the test - this measure is designed to detect any genuine distress (due to risk of excessive dehydration or weight loss) the patient may experience, and to guard against surreptitious drinking, which will influence the test interpretation.

4.2.1 Protocol

Day 1 - 18:00 h

If mild DI is suspected, the patient should be given a meal with one small glass of fluid. No food or water should be allowed after this until the test is completed. If severe DI is likely, free fluids (not tea, coffee or alcohol) and a light breakfast should be allowed prior to the test.

Day 2 - 08:00 h

Weigh the patient. The bladder should be emptied and the urine collected: record the urine volume passed. Blood should be collected. Both samples should be sent to the laboratory and urine and serum osmolality measured. If the urine osmolality is ≥750 mOsm/kg and the serum osmolality is normal (275-295 mOsm/kg) then the patient has demonstrated adequate urinary concentration and the test should be stopped.

If the urine osmolality is <750 mOsm/kg then the test should continue. Urine and blood samples should be collected hourly over the next 8 h, for urine and serum osmolality, and

urine volume should be documented. If adequate urinary concentration (urinary osmolality ≥750 mOsm/kg) is achieved at any time the test may be stopped. Patients must be weighed every 2 h.

Caution: if body weight falls by >3% or the serum osmolality rises >300 mOsm/kg at any point in the test the patient should be given access to fluids and be subjected to the vasopressin test (see below).

DI is diagnosed by a rise in serum osmolality ≥295 mOsm/kg without appropriate urinary concentration (<750 mOsm/kg).

Day 2 - 16:00 h (or as soon as serum osmolality ≥295 mOsm/kg)

Give 20 μg synthetic vasopressin (DDAVP, desmopressin) intranasally (2 sprays), or give 2 μg intramuscularly. Allow limited access to fluids (up to twice the volume of urine passed during the test), as the patient will be at risk of developing profound hyponatraemia. Collect urine samples hourly over the next 4 h and measure volume and osmolality.

Adequate concentration of urine after DDAVP indicates CDI, although lesser responses are occasionally seen in partial defects, whereas lack of concentration indicates NDI.

Failure to concentrate either urine or serum by the end of the test is non-diagnostic but usually represents primary polydipsia: such patients may require a period of pre-water deprivation test fluid restriction to correct medullary hypoosmolarity before achieving adequate urinary concentration.

Caution: exposure to DDAVP can be dangerous sometimes in psychogenic polydipsia, as the patient may suffer from overhydration some hours afterwards if fluid intake is not curtailed.

4.2.2 Interpretation of results

Post-dehydration osmolality (mOsm/kg)		Post DDAVP osmolality (mOsm/kg)	Diagnosis
Serum	**Urine**	**Urine**	
275-295	≥750	≥750	Normal
≥295	<300	<300	Nephrogenic DI
≥295	<300	≥750	Cranial DI
≥295	<750	<750	Partial CDI or NDI
<295	<750	<750	Primary polydipsia

5. Consultation and Approval

East Kent Hospitals University NHS Foundation Trust is the key stakeholder for this guideline.

Consultation has been through e-mail between clinical biochemistry staff and Trust consultant endocrinologists (Dr S Joseph – clinical lead, Endocrinology). Copies of correspondence are held on the shared drive.

6. Review and Revision Arrangements

Two years from implementation date, by author.

7. Training

Dissemination to relevant staff within Pathology via Q Pulse. Dissemination to users of the service via documentation hosted in the healthcare professional zone of Trustnet. Information may also be contained within the Pathology MicroGuide.

8. Document Control including Archiving Arrangements

Archive of this document will be through QPulse.

9. Monitoring Compliance

Within the Trust, compliance with this guideline must rest with the requesting Care Groups with vetting of requests in Clinical Biochemistry. Compliance will also be subject to occasional audits within Clinical Biochemistry.

10. References and Associated Documents

a) Ali S, Allum M *et al*. Imperial Centre for Endocrinology. Endocrinology Handbook 2018; 62-65.
b) Baylis PH. Medicine International 1993; 21: 189-196.
c) Bichet DG. Evaluation of patients with polyuria. 2019. UpToDate. Retrieved August 12, 2020 from https://www.uptodate.com/contents/evaluation-of-patients-with-polyuria#H232583011.

11. Appendices

Appendix A – Template for Water Deprivation Test Results

Patients name:					
Hospital no.:					
Date of test:					
Time test started:					
Test time	Real time	Body weight (kg)	Urine volume (mL)	Urine osmolality (mOsm/kg)	Plasma osmolality (mOsm/kg)
0 h					
Calculated weight - 3% =					
1 h		-			
2 h					
3 h		-			
4 h					
5 h		-			
6 h					
7 h		-			
8 h					
Give vasopressin if indicated					
9 h					
10 h					
11 h					
12 h					