

syzygy

Copeptin test for patients with polyuria-polydipsia syndromes

Dr Caroline Bachmeier, Chemical Pathology Registrar, Sullivan Nicolaides Pathology

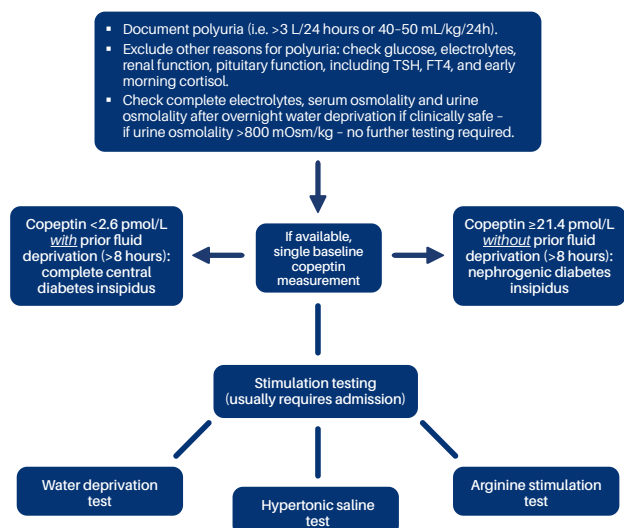
Arginine vasopressin (AVP) or anti-diuretic hormone (ADH) plays a key role in fluid balance homeostasis. However, AVP is notoriously difficult to measure. It is unstable and presents significant challenges for sample collection, transport, processing, and analysis. Copeptin is co-secreted with AVP, is stable in plasma, and performs better analytically. It closely correlates with AVP and is therefore an excellent surrogate marker in differentiating between diabetes insipidus and primary polydipsia. Sullivan Nicolaides Pathology now offers a copeptin test for patients with polyuria-polydipsia syndromes.

Copeptin (a 145 amino acid peptide) and arginine vasopressin (AVP) are derived from a common precursor molecule produced in the paraventricular and supraoptic nuclei of the hypothalamus. This precursor molecule – prepro-AVP – is transported to the posterior pituitary and spliced to AVP, neurophysin and copeptin during transport. Copeptin is released from the posterior pituitary gland in equimolar amounts to AVP and in response to the same stimuli, which include an increase in blood osmolality and/or decrease in blood volume. The physiological function of AVP is to maintain fluid balance and vascular tone. AVP binds to its receptor in the kidneys and leads to incorporation of aquaporin-2 channels, resulting in water reabsorption. It also increases vascular tone via peripheral receptors in the smooth vasculature. The function of copeptin is still under investigation.¹

Testing

Sullivan Nicolaides Pathology now offers a copeptin test on the BRAHMS KRYPTOR analyser using the unique TRACE™ Technology.

Testing pathway for polyuria and polydipsia



Polyuria and polydipsia syndromes are a common problem in clinical practice with the main entities being nephrogenic and central diabetes insipidus (DI), and primary polydipsia. Once polyuria (>3 L/24h) has been confirmed, causes such as hyperglycaemia, electrolyte abnormalities, and renal dysfunction should be ruled out, and thyroid function and cortisol should be checked.

A paired urine and serum osmolality with sodium should be measured, together with a baseline copeptin after overnight fluid restriction if clinically safe to do so.^{1,2}

Interpretation of results

Recent studies have shown that fasted baseline copeptin concentrations of <2.6 pmol/L make complete central DI very likely, whereas random concentrations of >21.4 pmol/L make nephrogenic DI very likely.¹⁻³ A copeptin measurement may obviate the need for time-consuming stimulatory tests. It is difficult to differentiate partial central DI from primary polydipsia with copeptin alone, and stimulatory tests, such as the hypertonic saline test, are still required to make this diagnosis.⁴ Recent studies have also demonstrated an exciting new technique of measuring copeptin after pituitary surgery to predict the risk of central DI.^{5,6}

Copeptin test information

What to request	All copeptin requests should be accompanied by a measured serum osmolality.
Sample type	1 x serum (SST).
Collection	Any SNP collection centre.
Transport	Allow specimen to clot, then centrifuge. Store at 2-8 °C.
Test turnaround	Results available within one week from receipt of specimen.
Cost	A test fee of \$125 will apply. Medicare rebate is not available for this test.

References

- ¹Christ-Crain M, Fenske W. Copeptin in the diagnosis of vasopressin-dependent disorders of fluid homeostasis. *Nat Rev Endocrinol*. 2016;12(3):168-176.
- ²Nigro N, Grossmann M, Chiang C, Inder WJ. Polyuria-polydipsia syndrome: a diagnostic challenge. *Intern Med J*. 2018;48(3):244-253.
- ³Refardt J, Winzeler B, Christ-Crain M. Copeptin and its role in the diagnosis of diabetes insipidus and the syndrome of inappropriate antidiuresis. *Clin Endocrinol (Oxf)*. 2019;91(1):22-32.
- ⁴Fenske W, Refardt J, Chifu I, et al. A Copeptin-Based Approach in the Diagnosis of Diabetes Insipidus. *N Engl J Med*. 2018;379(5):428-439.
- ⁵Winzeler B, Zweifel C, Nigro N, et al. Postoperative Copeptin Concentration Predicts Diabetes Insipidus After Pituitary Surgery. *J Clin Endocrinol Metab*. 2015;100(6):2275-2282.
- ⁶Vanasuntorn A, Hansasuta A, Chailurkit LO, Sriprapradang C. Postoperative Copeptin as a Biomarker for Development of Diabetes Insipidus Following Hypothalamic-Pituitary Surgery. *Endocr Pract*. 2021;27(5):463-470.



Better clinical management for salivary gland tumours with the Bethesda-style Milan reporting system

Diagnosing salivary gland tumours can often be challenging due to cellular diversity and heterogeneity. Morphological overlap between different tumours may also add further complexities to diagnosis. To provide better clinical management for salivary gland tumours, and to standardise reporting, we have adopted the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC).

The MSRSGC was developed with support from the American Society of Cytopathology and the International Academy of Cytology, and comprises of six diagnostic tiers. It conforms with a Bethesda-style reporting system with uniform terminology and risk stratification.

MSRSGC is a tiered reporting system with six diagnostic categories		
Category	Diagnosis	Risk of Malignancy (ROM)
i.	Non-diagnostic	25%
ii.	Non-neoplastic	10%
iii.	Atypia of undetermined significance (AUS)	20%
iv.	A. Neoplasm – Benign B. Salivary gland neoplasm of uncertain malignant potential (SUMP)	<5% 35%
v.	Suspicious for Malignancy	60%
vi.	Malignant	90%

Reporting Risk of Malignancy

It should be noted that the Risk of Malignancy (ROM), as categorised above, may be an overestimation as it is based on surgically excised specimens. The ROM may also be impacted by publication bias, patient demographics and institutional referral patterns.

Given this, we will not initially routinely provide the ROM in reports. However, referrers are encouraged to contact the reporting pathologist should they wish to know the reporting ROM.

The actual ROM is expected, in practice, to be in the mid-range of what is reported above. Our aim is to correlate our FNA findings with histologic outcomes (and other clinical follow-up) to provide a more accurate ROM.

If you have any questions or feedback regarding the MSRSGC, please contact your medical liaison manager on **1300 767 284** or email client.services@snp.com.au

Pathologist profile



Dr Tanya Robb BSc(Hons) MBBS FRCPA

Dr Tanya Robb is a consultant histopathologist at our Bowen Hills laboratory where she reports on gynaecological and gastrointestinal pathology, and cytology.

Dr Robb graduated in Medicine from The University of Queensland in 2004 having first gained honours in a Bachelor of Science. She undertook internship at the Cairns Base Hospital, followed by residency at the Alfred Hospital, Melbourne.

Pursuing a preference for diagnostic medicine, she returned to Brisbane in 2007 to take up advanced training in anatomical pathology. This was completed at various hospitals and institutions in south-east Queensland, including private pathology. She was awarded Fellowship of the Royal College of Pathologists of Australasia in February 2013.

Dr Robb returned to Melbourne as a histopathologist at Melbourne Pathology, reporting a wide range of surgical pathology, including gynaecological oncology and gastrointestinal specimens. She joined SNP in 2022 and participates in regular multidisciplinary clinical meetings held to review and discuss oncology cases. She maintains an active interest in training pathology registrars.

Dr Robb is published in her field of interest, most notably a paper in the International Journal of Gynecological Pathology on a rare case of primary apocrine adenocarcinoma of the ovary.

Dr Robb is available for consultation.

P (07) 3377 8404 | **E** tanya_robb@snp.com.au

Changes to HPV self-collections July 2022

- SNP is fully validated to carry out the self-collect HPV testing using the red-topped FLOQ swab.
- When self-collection is determined as the preferred sampling method, it is optimal that the sample be collected onsite in the clinic.
- We supply HPV self-collect kits with illustrated step-by-step instructions. Please note, kits supplied are for HPV self-collects only; separate swabs are required for additional tests.
- Self-collected samples **cannot** be used for Test of Cure or symptomatic patients; these women need a co-test, HPV and cytology, performed simultaneously.
- The National Cancer Screening Register will record the method of sampling in the patient's file.

CST resources

Updated CST resources for clinicians and patients are available on request. To order, please contact your medical liaison manager on **1300 767 284** or email client.services@snp.com.au



Self-collected HPV test clinician update including routine testing flowchart



HPV self-collect kit



CST patient brochure