Information for Clinicians

Biochemistry Department

Waking Salivary Cortisone for Investigation of Adrenal Insufficiency

Background

Saliva contains cortisol that is derived from the serum circulation; this is converted to salivary cortisone due to high levels of 11β-hydroxysteroid dehydrogenase type 2 in the salivary glands. Salivary cortisone correlates well with serum cortisol levels and is detectable even at low serum cortisol concentrations. Therefore, measurement of cortisone in waking saliva collections can be used as an alternative to the Short Synacthen Test (SST) to assess adrenal function.

Waking salivary cortisone (WSC) samples can be collected by patients at home and this test avoids the need for outpatient attendance for SST in a large proportion of patients. However, note that approximately 30% of patients who have WSC tested may receive results in the equivocal range, requiring follow-up with SST.

Analysis of WSC is not performed on site at RUH and results will take approximately two weeks to be reported. WSC should NOT be performed where urgent assessment of adrenal function is required; please perform an urgent SST instead.

Patient suitability

WSC is only available for patients under the care of the RUH Endocrinology team.

Do not perform WSC in preference to SST in:

- patients taking supraphysiological doses of steroids
  (e.g. hydrocortisone >25 mg/day, prednisolone >5 mg/day or equivalent)
- patients with 9am serum cortisol <150 nmol/L
- patients with bleeding mouth, gums or lips
- night shift workers
- active infection
- pregnancy
- alcoholism
- severe liver disease
- patients unable to produce adequate saliva
- <16 year olds

Patient preparation

Patients should be provided with a pre-labelled (Millennium barcoded) salivette tube along with instructions on how to perform the collection (Appendix).

Patients should be asked to collect the WSC sample immediately on waking at their usual time and to follow these instructions prior to sample collection:

- Do not smoke/vape
- Do not eat or drink
- Do not clean teeth or use mouthwash
- Do not take any medications (if on steroids see below)

Steroid medication	Omission dose/period before sample collection
Hydrocortisone	Omit evening dose prior to morning collection AND delay morning dose until after sample collection
Prednisolone	Omit for 24h before sample collection
Dexamethasone	Omit for 72h before sample collection

If on steroids, patients should omit their doses as detailed above prior to the planned morning sample collection and delay their morning dose of steroid until after the saliva sample has been collected.

Once the saliva sample has been collected all medications should be taken as usual.

The saliva sample should be transported to the RUH laboratory on the day of sample collection; this can be via handing it in at the patient's local GP surgery in the morning following sample collection.

Interpretation

Results should be interpreted using the following thresholds:

Salivary Cortisone	Interpretation	Follow-up
<7 nmol/L	Adrenal insufficiency likely	Steroid replacement
7 – 24 nmol/L	Equivocal result	Perform SST
≥25 nmol/L	Adrenal insufficiency unlikely	Discharge

Literature reports a WSC <7 nmol/L has a specificity of 97% and positive predictive value (PPV) of 95% when compared to standard SST. WSC ≥17 nmol/L has a sensitivity of 97% for the exclusion of adrenal insufficiency but this is increased to 99% at WSC ≥25 nmol/L.

Test limitations

There is a risk of sample contamination in patients taking oral hydrocortisone; this can be mitigated by omitting the previous evening dose and delaying the morning dose of hydrocortisone until after the saliva is collected. The laboratory will usually be able to determine if sample contamination is likely as a higher concentration of salivary cortisol vs salivary cortisone will usually be observed (usually salivary cortisone concentrations are 6x higher than salivary cortisol concentrations).

Contamination of the salivary sample with blood will also increase salivary cortisol levels relative to cortisone, due to the blood concentrations of cortisol being approximately 4x higher than blood cortisone.

If sample contamination is suspected, the salivary cortisone concentration SHOULD NOT be used to exclude adrenal insufficiency; a repeat WSC or SST should be performed.

References

Backlund, N. *et al.* Salivary Cortisol and Cortisone Can Circumvent Confounding Effects of Oral Contraceptives in the Short Synacthen Test. J Clin Endo Metab. 2024:109(7): 1899-1906
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Amendment History

Issue	Status	Date	Reason for Change	Authorised
1.0	Approved	April 2025	New guideline	Moya O'Doherty

Appendix – Patient Instructions

Royal United Hospitals Bath NHS
NHS Foundation Trust

Instructions for Collection of Saliva Samples for Waking Salivary Cortisone and Cortisol

Please collect your saliva upon waking at your usual time in the morning.

Prior to sample collection:

- Do not smoke/vape
- Do not eat or drink
- Do not clean teeth or use mouthwash
- Do not take any medications (if on steroids omit these before the test as instructed by your doctor or endocrine nurse specialist)

- Once the sample has been collected you may continue with the above as required.

Collect the sample Mon-Thurs AM and take the sample to the GP on the morning of collection.

Collecting your saliva:

Step 1: Hold the tube and remove the stopper.

Step 2: Remove swab and place in mouth.
Gently chew for at least 2 minutes until swab is saturated.
(Alternatively you can discard the swab and passively drool into the tube, before securing with the stopper).

Step 3: Return swab to the tube (plus any additional saliva in mouth) and replace the stopper.

Step 4: Write the date & time (24h clock) you took the sample clearly on the tube. Check your name and DOB are correct.

Step 5: Then take the sample enclosed in the bag provided to your GP surgery for delivery to the laboratory.

Alternatively the sample may be handed in at the RUH Pathology Laboratory, B36.

If you have any questions please contact the duty biochemist on 01225 824050.