VibrantWellness

Serum, Saliva, or Urine?

Quick Comparison Sheet

Serum, Saliva & Urine Quick Glance Hormone Test Comparison

Method	Baseline Hormones	Diurnal Cortisol/HPA Axis Curves	Hormone Metabolites	Oral/Pellet/ Patch HRT	Transdermal Progesterone	Sublingual HRT
Serum	✓			✓[a]		✓[c]
Saliva	✓	✓		✓[a]	✓	
Urine	✓	✓	✓	✓[a,b]		

[a] *Need to account for timing of testing in relation to oral HRT intake to assess dosing. Consider combining methodologies for the most comprehensive representation.*

[b] *Oral progesterone is not measured directly in urine testing, progesterone metabolites are measured.*

[c] *Need to account for timing of testing in relation to sublingual HRT.*

Serum Hormone Testing Strengths

- Defaults to measure total hormone, bound and unbound (although some free hormone tests can be obtained in serum)
- Can be used for baseline monitoring of hormones and comprehensive diagnostic work-ups
- Can collect for thyroid, SHBG and other tests in addition to sex steroids at the same collection
- Current standard of care to monitor oral HRT/pellet/patch

Serum Hormone Testing Limitations

- Transdermal HRT is underrepresented[1]
- Cortisol is not tested in a diurnal pattern; HPA axis curves not available for assessment
- Does not measure most free unbound hormones or metabolites
- Oral progesterone levels may not be accurately captured due to fast metabolism
- Typically only offers one point in time measuring

Serum Quick Glance Hormone Test Comparison

Method	Baseline Hormones	Diurnal Cortisol/HPA Axis Curves	Hormone Metabolites	Oral/Pellet/ Patch HRT	Transdermal Progesterone	Sublingual HRT
Serum	✓			✓[a]		✓[d]

[a] *Need to account for timing of testing in relation to oral HRT intake.*

[d] *Need to account for timing of testing in relation to sublingual HRT.*

Salivary Hormone Testing Strengths

- Reflects free, bioavailable hormone rather than total, bound hormone[2]
- More representative of tissue levels of topical hormones than serum or urine, best testing method to prevent overdosages of topical creams and gels[1–3]
- Research-based efficacy for adrenal cortisol monitoring including diagnosis of Cushing's disease, also helpful for sub-optimal levels, hypocortisolemia and HPA axis dysregulation[4,5]
- LC-MS/MS assay methodology is highly sensitive for even low levels of estradiol in saliva[2]
- Convenient to collect sample at home
- Pooled samples combine results from 4 points throughout the day rather than single time point collection
- Can aid in measuring bioavailable baseline hormone levels prior to HRT, although serum may be also advised for full diagnostic workups

Salivary Hormone Testing Limitations

- Not the preferred method to test when using HRT in sublingual suspensions/troche lozenges due to direct contamination of salivary reservoir with HRT.
- Does not measure metabolites to evaluate estrogen and other hormone metabolism
- Potential interactions with food, drinks, or blood from recent tooth brushing – must avoid these with testing
- Only utilized in steroid-based hormones
- Can be difficult to collect enough salivary for testing in patients with poor salivary flow

Saliva Quick Glance Hormone Test Comparison

Method	Baseline Hormones	Diurnal Cortisol/HPA Axis Curves	Hormone Metabolites	Oral/Pellet/ Patch HRT	Transdermal Progesterone	Sublingual HRT
Saliva	✓	✓		✓[a]	✓	

[a] *Need to account for timing of testing in relation to oral HRT intake.*

Urine Hormone Testing Strengths

- Measures hormone metabolites which reflect metabolism and clearance of hormones[6,7] and related enzyme pathways
- Can accurately reflect baseline hormone levels (exception: Urinary T levels will be absent with genetic snp UGT2B17)
- Measures 8-OHDG and diurnal melatonin (via MT6s metabolite), BPA, HPA axis dysregulation
- Can assess for risks specifically associated with estrogen metabolites, i.e., 2-OH-E2 vs 4-OH-E2 pathways[6]
- Metabolites for cortisol and cortisone can shed light on cortisol/cortisone dynamics in tissues

Urine Hormone Testing Limitations

- When using excretory products for measuring, there can be a range of interpretations.
    - Low excreted urine hormone levels may suggest either low production or increased tissue uptake
    - High levels may reflect either tissue saturation or overproduction
    - Free cortisol can be converted at kidney to cortisone, thus urinary cortisol can be underrepresented
- Need to control for time of testing in relation to oral HRT intake to avoid false elevations from 1st pass metabolism
- May underrepresent transdermal HRT[8]
- Vaginal HRT may contaminate urine samples
- May be inaccurate in those with renal disease/creatinine irregularities

Urine Quick Glance Hormone Test Comparison

Method	Baseline Hormones	Diurnal Cortisol/HPA Axis Curves	Hormone Metabolites	Oral/Pellet/ Patch HRT	Transdermal Progesterone	Sublingual HRT
Urine	✓	✓	✓	✓[a,c]		

[a] *Need to account for timing of testing in relation to oral HRT intake.*

[c] *Oral progesterone is not measured directly in urine testing, progesterone metabolites are measured*

References

1. Du JY, Sanchez P, Kim L, Azen CG, Zava DT, Stanczyk FZ. Percutaneous progesterone delivery via cream or gel application in postmenopausal women: a randomized cross-over study of progesterone levels in serum, whole blood, saliva, and capillary blood. *Menopause.* 2013;20(11):1169-1175. doi:10.1097/GME.0b013e31828d39a2
2. Stanczyk FZ, Matharu H, Winer SA. Bioidentical hormones. *Climacteric.* 2021;24(1):38-45. doi:10.1080/13697137.2020.1862079
3. Stanczyk FZ. Treatment of postmenopausal women with topical progesterone creams and gels: Are they effective? *Climacteric.* 2014;17(Suppl 2):8-11. doi:10.3109/13697137.2014.944496
4. Papanicolaou DA, Mullen N, Kyrou I, Nieman LK. Nighttime salivary cortisol: A useful test for the diagnosis of Cushing's syndrome. *J Clin Endocrinol Metab.* 2002;87(10):4515-4521. doi:10.1210/jc.2002-020534
5. Kim YJ, Kim JH, Hong AR, et al. Stimulated Salivary Cortisol as a Noninvasive Diagnostic Tool for Adrenal Insufficiency. *Endocrinol Metab.* 2020;35(3):628-635. doi:10.3803/enm.2020.707
6. Denver N, Khan S, Homer NZM, MacLean MR AR. Current strategies for quantification of estrogens in clinical research. *J Steroid Biochem Mol Biol.* 2019;Sep(192):105373.
7. Kaleta M, Oklestkova J, Novák O SM. Analytical Methods for the Determination of Neuroactive Steroids. *Biomolecules.* 2021;Apr 9;11(4):553.
8. O'Leary P, Feddema P, Chan K, Taranto M, Smith M, Evans S. Salivary, but not serum or urinary levels of progesterone are elevated after topical application of progesterone cream to pre-and postmenopausal women. *Clin Endocrinol (Oxf)*. 2000 Nov;53(5):615-20. doi: 10.1046/j.1365-2265.2000.01130.x. PMID: 11106923.