

Which collection method provides the most comprehensive and valid information?

TESTING MATRIX	No Supplementation		With Hormone Replacement Therapy						
	Sex Hormones	Adrenal	Oral Pg	Oral (other)	Sublingual	Vaginal	Pellet/Inj.	Cream (skin)	Gel (skin)
Serum	B +Well accepted and reliable methods - No metabolites	D No diurnal free cortisol	F Inaccurate# and too Fast*	B +Works for DHEA, estrogens - No metabolites	D Too Fast* (back to baseline in <3hrs)	C Rise and fall is unpredictable, so timing is difficult	B +Well accepted and reliable methods - No metabolites	D Values under-represent some tissue levels	B Increases are more significant than with creams
Saliva	C + Good for tracking levels thru cycle - Difficult analysis No metabolites	B +Diurnal free cortisol - No metabolites	F Inaccurate# and too Fast*	B- Difficult analysis No metabolites	F Contamination lasts longer than blood levels are elevated	D Rise and fall is unpredictable, so timing is difficult	B- - Difficult analysis No metabolites	D D % Values are too variable, change dramatically with different application sites, and do not represent systemic exposure	
24-Hour Urine	A +Mass spectrometry (accurate) Includes metabolites - Difficult collection	C +Metabolites - No diurnal cortisol Often "total" not "free"	C Metabolites of marginal value	B- Difficult to avoid 1st-pass metabolism (skip dose day of test)	C Difficult to avoid 1st-pass metabolism from oral intake	D +Works for Pg - Estrogen/Test contamination	A Hormones and metabolites	D Values under-represent some tissue levels	B Increases are more significant than with creams
Dried Urine	A Mass spectrometry (accurate) Includes metabolites Easy collection	A+ IDEAL OPTION Diurnal Cortisol AND Metabolites!	C Metabolites of marginal value	B- Difficult to avoid 1st-pass metabolism (skip dose day of test)	C Difficult to avoid 1st-pass metabolism from oral intake	B+ IDEAL OPTION free hormone contamination is removed	A Hormones and metabolites	D Values under-represent some tissue levels	B Increases are more significant than with creams

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Cortisol interpretation guide

Free Cortisol	Normal	High	High	Normal
Cortisol Metabolites	Normal	High	Very High	High
Metabolism Rates	Not High	Not High	High	High
Interpretation	Normal Function	This is a healthy response to stress. HPA axis is up-regulated, but may not be chronic to the point of causing dysfunction. Focus should be on lowering cortisol.	This implies stress or HPA stimulation that is potentially long-term as metabolism rates have been increased.	Metabolism rates increased perhaps after long-term stress, or from insulin resistance or obesity or another reason.
Clinical Implication	Healthy not stressed	Positive response to stress	Negative response to stress	Mild adrenal exhaustion

Free Cortisol	Normal	High	Low	Low
Cortisol Metabolites	Low	Normal or Low	Normal or High	Low
Metabolism Rates	Low	Low	High	Not High
Interpretation	Cortisol is not cleared as it should be. This may not be a problem, but could be a sign of nutrient deficiencies or hypothyroidism	High cortisol without an overactive HPA-axis. Cortisol not clearing, suggesting sluggish metabolism induced hypercortisol. Possible nutrient deficiency or hypothyroidism.	Cortisol deficiency caused at least partly by increased metabolism. Chronic fatigue syndrome may present this way	True adrenal insufficiency
Clinical Implication	Adrenal exhaustion (this state shows as "normal" in saliva testing)	Adrenal exhaustion (NOT caused by overactive adrenals, would not be evident in saliva testing)	extreme adrenal exhaustion	complete adrenal exhaustion

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