



DISCOVER BEAUTY IN BALANCE.

Do you suspect hormone issues are negatively impacting your patient's health?

Rocky Mountain Analytical® is now offering **Comprehensive Hormone Insights™ (CHI)**. This urine test provides important information regarding hormone production and metabolism, to provide insights into your patients' overall hormone balance.

Find out why your colleagues are using CHI

CHI Provides Insight Into Patient Symptomatology

Comprehensive Hormone Insights provides detailed urine analysis that measures steroid hormones, steroid hormone metabolites and assesses diurnal cortisol levels.

Urine steroid hormone testing can provide important information that may be relevant for many health conditions including:

Women

- Breast cancer
- Endometrial cancer
- Metabolic syndrome (MetS)
- Polycystic ovary syndrome (PCOS)
- Endometriosis
- Osteoporosis/bone loss
- Infertility
- Premenstrual syndrome (PMS)
- Premenstrual dysphoric disorder (PMDD)
- Fatigue
- Sleep difficulties
- Inflammatory disorders

Men

- Metabolic syndrome (MetS)
- Benign prostatic hyperplasia (BPH)
- Prostate cancer
- Gynecomastia
- Erectile dysfunction (ED)
- Osteoporosis, bone loss
- Fatigue
- Sleep difficulties
- Inflammatory disorders

Order CHI to receive a comprehensive report to help understand health conditions related to steroid hormone regulation.

CHI Provides a Detailed Assessment of Your Patients' Hormones

The following hormones and hormone metabolites are included in CHI

Hormone Categories	Clinical Utility
Cortisol and cortisone metabolites such as: <ul style="list-style-type: none">• 5α-tetrahydrocortisol (5α-THF)• 5β-tetrahydrocortisol (5β-THF)• 5β-tetrahydrocortisone (5β-THE)	<ul style="list-style-type: none">• Glucose and insulin metabolism• Fat deposition and adiposity• Insight into burnout, chronic illness, acute stress, and balance between anabolic/catabolic processes• Insight into thyroid issues
Conjugates such as: Cortisol sulfate, cortisol glucuronide, testosterone glucuronide, estrone sulfate, DHEA sulfate, and DHEA glucuronide	<ul style="list-style-type: none">• Provide insight into effects of 'stored' hormone and liver function related to hormone metabolism.• May provide insight into inflammation
Androgens and 17-ketosteroids such as: <ul style="list-style-type: none">• Testosterone• Dihydrotestosterone (DHT)• Androsterone• Etiocholanolone• Dehydroepiandrosterone (DHEA)	<ul style="list-style-type: none">• Infertility• Polycystic ovary syndrome (PCOS)• Metabolic syndrome (MetS)• Benign prostatic hyperplasia (BPH)• Thyroid issues
Progesterone metabolites: <ul style="list-style-type: none">• α-pregnanediol• β-pregnanediol• Allopregnanolone Precursor steroid: <ul style="list-style-type: none">• 17OH-pregnenolone	<ul style="list-style-type: none">• Mood disorders• Thyroid issues• PCOS• Breast tenderness• Uterine fibroids
Estrogen and metabolites such as: <ul style="list-style-type: none">• Estrone (E1); Estradiol (E2); Estriol (E3)• Estrone sulfate (E1S)• Methylated and hydroxylated estrogens	<ul style="list-style-type: none">• Menstrual disorders• Risk of estrogen-sensitive cancers• Prostate cancer risk• Breast enlargement or tenderness• Uterine fibroids
Melatonin metabolite: <ul style="list-style-type: none">• 6-sulfatoxymelatonin	<ul style="list-style-type: none">• Insomnia• Premenstrual dysphoric disorder (PMDD)• Breast cancer risk
8-hydroxy-2-deoxyguanosine (8OH2dG)	<ul style="list-style-type: none">• An important biomarker of oxidative stress

NOTE: This is a summary, rather than a detailed list of analytes reported in CHI.

CHI measures a wide range of metabolites to provide a more complete picture of the hormonal health of your patient.

How Does CHI Stack up Against Other Urine Steroid Hormone Tests?



Superior reporting of results

- Heat map
 - Immediate visual identification of which hormone pathways are **hot** (i.e., overactive) or **cold** (i.e., underactive)
 - Allows clinicians to identify hormonal issues at-a-glance
- Custom interpretation of patient results
 - CHI includes a detailed, patient-specific commentary to guide the interpretation of patient hormone levels and help identify possible causes of symptoms
- Percentiles reported, in addition to individual results
 - Percentiles show how patients' results compare to a clinically-well population
- More in-depth analysis of results via ratios



Liquid urine samples

- Collection of liquid urine can be done discreetly
- Peer-reviewed literature supports liquid urine steroid hormone analysis



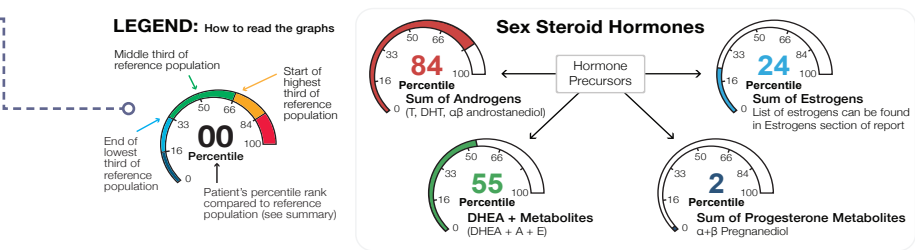
4-point pooled urine samples

- 4-point samples compared to a 24-hour collection
 - Cortisol diurnal variation was previously only measurable in saliva and serum. The daytime urine samples show the same pattern as saliva, and also provide information on cortisol metabolism
 - 4-point samples eliminate the need for a cumbersome 24-hour urine collection
 - Results from the pooled sample derived from the 4-point samples can be equated to results from a 24-hour collection

How to Read a CHI Report

SUMMARY DIALS

The first page of the report summarizes key hormone measures including: androgens, estrogens, progesterone metabolites, DHEA & metabolites, 8OH2dG, 6-sulfatoxymelatonin and the ratio of cortisol to testosterone.



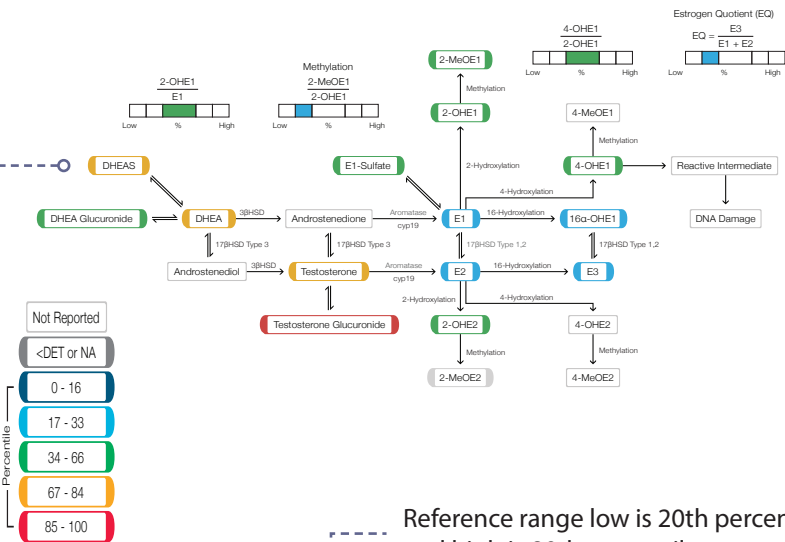
HORMONE CATEGORY

Each hormone category has its own heatmap and corresponding bar graphs for individual analytes.



HEATMAP

Hormone endcap colour immediately identifies which hormone levels are high, high normal, normal, low normal and low.



RESULTS & RANGES

This section reports the results, ranges and graphs for the percentiles of individual analytes and sums/ratios. Range applied is specific to patient: male, female and whether luteal, follicular or post-menopausal.

ESTROGENS										
Analyte	Result	Range	Units	0%	16%	33%	66%	84%	100%	Range Applied
Estrone (E1)	6.7	5.3 - 15	ng/mL						31%	d21
Estradiol (E2)	2.4	2.3 - 5.5	ng/mL						25%	d21
Estriol (E3)	7.2	6.7 - 39	ng/mL						24%	d21
E3/(E1 + E2)	0.79	0.65 - 2.7							26%	d21
2-Hydroxyestrone (2-OHE1)	6.0	3.0 - 12	ng/mL						41%	d21
2-OHE1/E1	0.89	0.38 - 0.99	ng/mL						66%	d21
2-Methoxyestrone (2-MeOE1)	1.5	0.79 - 4.5	ng/mL						39%	d21
2-MeOE1/2-OHE1	0.25	0.21 - 0.55							29%	d21
16a-Hydroxyestrone (16a-OHE1)	2.7	2.3 - 10	ng/mL						25%	d21
2-OHE1/16a-OHE1	2.2	0.43 - 2.6							69%	d21
4-Hydroxyestrone (4-OHE1)	0.98	0.53 - 2.1	ng/mL						41%	d21
4-OHE1/2-OHE1	0.16	0.13 - 0.26							40%	d21
2-Hydroxyestradiol (2-OHE2)	0.94	0.42 - 2.8	ng/mL						48%	d21
2-Methoxyestradiol (2-MeOE2)	< 0.30	0.085 - 4.1	ng/mL						<DET	d21
Estrone sulphate (E1-Sulphate or E1S)	0.95	0.45 - 2.0	ng/mL						55%	d21
Sum of Estrogens	28	27 - 87	ng/mL						24%	d21

COMMENTARY

Custom interpretation comments appear after each hormone category.

INTERPRETATION WHEN MULTIPLE ESTROGENS AND ESTROGEN METABOLITES ARE LOW
Many estrogenic hormones and hormone metabolites measured here are low. This pattern may still be quite clinically meaningful; however, prudence should be used when attempting to correlate and compare results via ratios. The clinician has to always bear in mind that the ratio may be less significant when the results making up the numerator and denominator are low compared to ratios constructed from results that are normal or elevated.

Unique & Important Metabolites & Ratios

Estrogen Ratios and Metabolites

Measurement, Ratio or Metabolite	Clinical Value
Ratio of 4-hydroxyestrone (4OHE1) to 2-hydroxyestrone (2OHE1)	Has been proposed as a marker of breast cancer risk. ¹
Ratio of 2OHE1 to Estrone (E1)	Provides insight into 2-hydroxylation: higher levels of 2OHE1 (relative to other hydroxylated estrones) may be associated with decreased cancer risk. ^{2,3,4,5,6}
Estrogen Quotient (Estriol (E3)/Estradiol (E2) + E1)	Research suggests that patients with low ratios may be at greater risk for estrogen-sensitive cancers. ⁷
Estrone Sulfate (E1S)	An important form of stored estrogen that provides insight into the impact of supplemented oral or sublingual estrogens on estrogen stores, and may also inform on sulfatase and sulfotransferase activity. ⁸
Sum of Estrogens	Provides a view into overall estrogen production, representing many estrogens and principle metabolites.

Cortisol Metabolism

Many of these ratios are unique to CHI, and all contribute to our understanding of the role of cortisol in health.

Measurement, Ratio or Metabolite	Clinical Value
Free Cortisol Profile	Informs on the cortisol day curve. A positive slope (rising) or a slope near zero (flattened) may be signs of burnout or chronic illness, while a steeply-negative slope (falling) may indicate anxiety or acute stress.
Activity of 11βHSD2	11βHSD2 converts cortisol to inactive cortisone, and when it is inhibited, free cortisol will typically be much greater than free cortisone. ^{9,10}
Ratio of Cortisol Metabolites to Cortisone Metabolites (α-THF + β-THF/THE)	Provides another view into 11βHSD2 activity.
Ratio of α-THF to β-THF	Provides insight into thyroid function, and decreased adrenocorticotrophic hormone (ACTH). ^{11,12,13}
Cortisol Conjugation Pattern	Provides insight into the proper interpretation of free cortisol results. Ability to conjugate hormones may be affected by liver function, presence of toxins, inflammation ¹⁴ , availability of conjugates, medications ¹⁵ and genetic polymorphisms.
Morning Cortisol Response	The Ratio of Free Cortisol (Morning) to Free Cortisol (Overnight) may be a surrogate for the salivary cortisol awakening response. ¹⁶
Overnight Cortisol Response	Ratio of Free Cortisol (Overnight) to Free Cortisol (Bedtime) provides insight into diurnal rhythm, with low ratios (near 1) found in both Addison's and Cushing's patients. ¹⁷
Ratio of Cortisol to Testosterone	Provides insight into the balance of anabolic (repair and growth) and catabolic (wear and tear) hormones.

Unique & Important Metabolites & Ratios

Unique or Important Metabolites

Measurement, Ratio or Metabolite	Clinical Value
17OH-pregnenolone	An intermediate metabolite essential for steroid hormone synthesis. Research shows 17OH-pregnenolone is an important precursor to DHEA and may help identify polycystic ovary syndrome (PCOS). ^{18,19}
Allopregnanolone	A progesterone metabolite that has been closely linked with premenstrual dysphoric disorder in the luteal phase ²⁰ , as well as depression in postmenopausal women. ²¹
8-hydroxy-2-deoxyguanosine (8OH2dG)	An important biomarker of oxidative stress, which has been implicated in numerous chronic diseases including: cardiovascular disease, depression, cancers, chronic fatigue and Parkinson's disease. ^{22,23,24,25,26}
6-sulfatoxymelatonin	The primary metabolite of melatonin, which has anti-oxidant anti-depressant, anti-inflammatory, pain-modulating, and neuroprotective effects. ^{27,28}
Conjugates	Provide insight into the effects of supplemented hormones, hormone storage, and liver function. ^{8,11}

Unique or Important Ratios

Measurement, Ratio or Metabolite	Clinical Value
Ratio of Testosterone to EpiTestosterone (T/Epi-T)	Provides insight into whether testosterone is being supplemented in men or women (supplementation increases testosterone, but not epi-testosterone).
Androsterone Excretion Ratio (Androsterone/Androsterone + Etiocholanolone)	May provide insights into thyroid function and alpha reductase activity. ²⁹
Methylation Capacity (2-methoxyestrogen (2MeOE1)/2-hydroxyestrone (2OHE1))	May help inform on catecholamine clearance, neurotransmitter balance and risk of estrogen-sensitive cancers.

Testing methods and techniques

- Liquid chromatography–mass spectrometry (LC-MS/MS) does not use hydrolysis, and measures both conjugated and free forms of the hormones, separately
- Gas chromatography–mass spectrometry (GC-MS/MS) numbers represent total hormone. After hydrolysis, all forms of hormone are converted to their unconjugated or 'free' form and measured via GC-MS/MS

CHI delivers clinically meaningful insights by reporting ratios, conjugates and sums.

CHI Can Benefit Patients like Nicole



Age: 53 year old female

BMI: 25 kg/m²

Current medications: Oral micronized progesterone 200 mg at bedtime

Relevant history: Nicole previously had disturbed sleep, which resolved when oral progesterone was prescribed. However, her sleep issues have recurred in the form of night sweats, trouble getting to sleep and frequent waking.

Primary complaints: Nicole presented to her doctor with complaints of significant sleep disturbance, mild acne and thinning hair.

Will estrogen therapy help relieve Nicole's symptoms?

Nicole's Saliva Hormone Test Results

Hormone	Status	Result	Range	Units	Range Applied
Estradiol	Within range	0.9	0.0 - 4.0	pg/mL	Endogenous postmenopausal range
Progesterone	Within range	110	50 - 150	pg/mL	Pg oral 6 to12 hrs (<=200mg)
Testosterone	Within range	21	15 - 45	pg/mL	Endogenous testosterone > 30 yrs
DHEAS	Within range	4.0	1.0 - 6.5	ng/mL	Female DHEAS 51-64 years
Cortisol AM	Within range	8.0	1.8 - 12	ng/mL	First sample:1st hour of waking
Hormone Therapies		Last Used			
Progesterone oral (200 mg)		9 hrs			

Clinical Summary

Nicole's estradiol is at the low end of the normal range, which means she might benefit from estrogen therapy. Progesterone is within normal range for a post-menopausal woman taking oral progesterone. Her other hormones are within normal range.

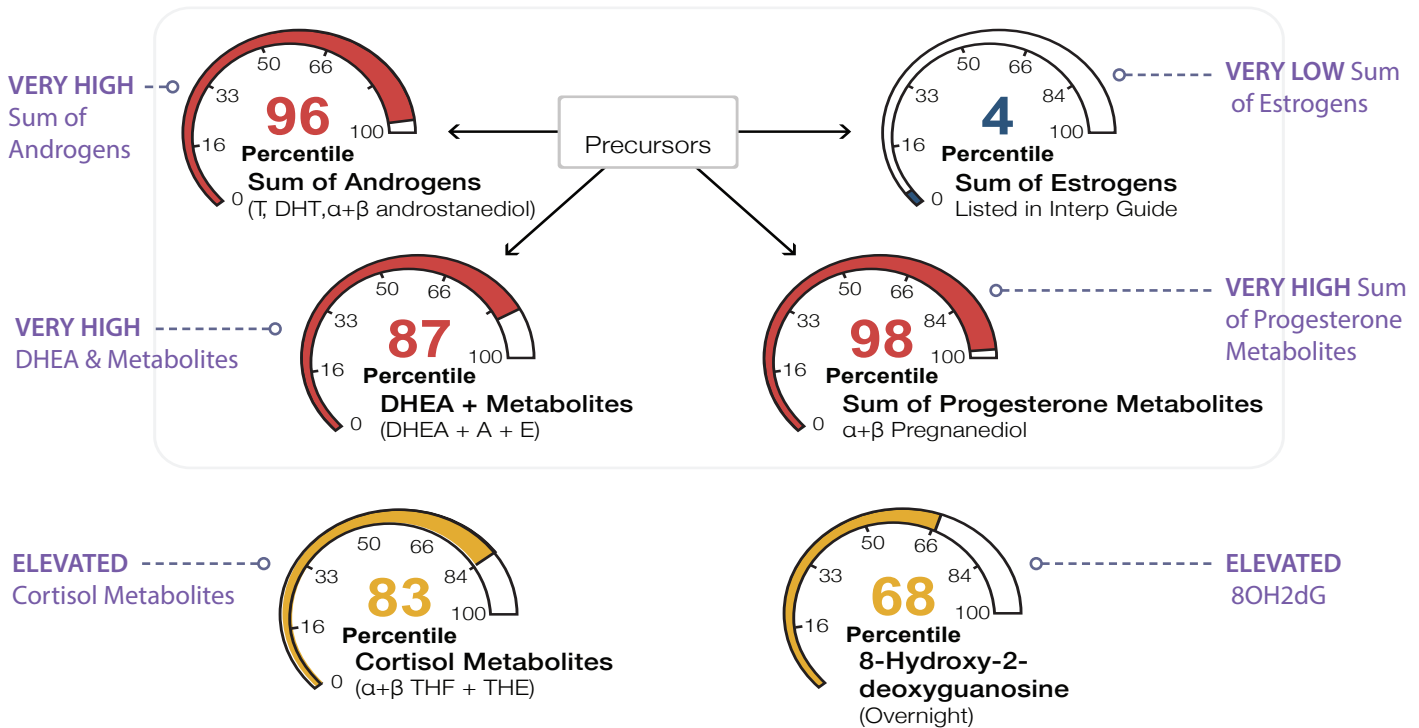
Recommendation: Comprehensive Hormone Insights™ (CHI)

CHI measures urine levels of parent hormones and metabolites. Because Nicole is considering supplementing with estrogens, her estrogen metabolism is of particular interest. A CHI test will assess how Nicole metabolizes estrogens to help manage the risks associated with estrogen replacement. CHI also reports 6-sulfatoxymelatonin, androgens and other hormones that may offer insight into causes of sleep disturbances, mild acne and thinning hair.

Both saliva and urine can identify low estrogen and diurnal cortisol. However, CHI provides additional insights into estrogen metabolism that could affect treatment recommendations.

Nicole's CHI Results

CHI SUMMARY PAGE (HMUS01)



Clinical Summary

Nicole has very high results for Sum of Androgens, DHEA & Metabolites, and Sum of Progesterone Metabolites, consistent with her prolonged use (more than one year) of high dose oral progesterone. Backdoor conversion to androgen and 17-ketosteroid metabolites can occur with excess progesterone, and the elevated levels of these metabolites may be the cause of Nicole's thinning hair and mild acne. Nicole's Sum of Estrogens is very low, as is expected based on her age and saliva hormone test results. Her Cortisol Metabolites are high, which might be contributing to sleep issues and her oxidative stress marker 8-OH2dG is elevated, which may contribute to health issues over the longer term. Ascribing clinical significance to estrogen metabolism ratios is ill-advised when estrogen metabolite levels are very low.

Possible Clinical Interventions*

- Reduce oral micronized progesterone from 200mg to 100mg at bedtime to decrease backdoor conversion of progesterone into testosterone.
- Recommend topical estrogens to alleviate night sweats and sleep disturbance.
- Undertake measures to reduce oxidative stress such as: antioxidants and hydrogenated water.
- Reduce cortisol levels, taking into account results on Cortisol Heat Map (not shown).
- It may be worthwhile to order a retest of CHI in 6 to 12 months to determine whether interventions to reduce backdoor conversion and lower cortisol and oxidative stress have been successful. Note, if Nicole uses topical estrogens, the levels of estrogen metabolites may not increase much, if at all. Topical hormones do not form significant metabolites.

* Interventions are for discussion purposes - CHI does not provide patient-specific treatment recommendations.

CHI Can Benefit Patients like Richard



Age: 64 year old male
BMI: 29 kg/m² Waist 44 inches
Current medications: Simvastatin, allopurinol, PPI, SSRI
Relevant history: Business executive, stressful career, non-smoker
Primary complaints: Richard presented to his doctor with complaints of: loss of interest in usual activities, “grumpiness”, difficulty losing weight, breast enlargement, constipation, fatigue, weakness, low sex drive, aches and pains.

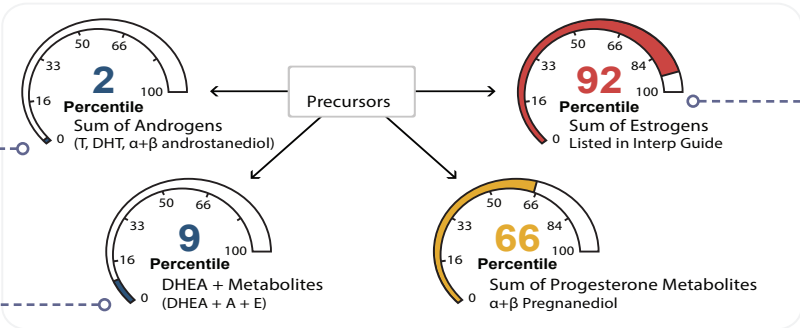
Is testosterone deficiency the cause of Richard's symptoms?

Richard's CHI Results

CHI SUMMARY PAGE (HMUS01)

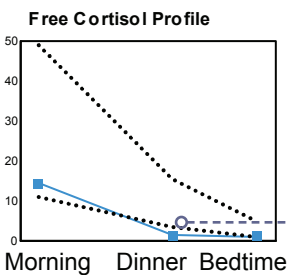
VERY LOW
Sum of Androgens

VERY LOW
DHEA & Metabolites

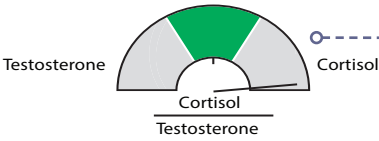
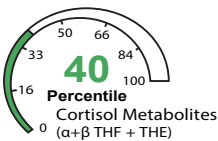


HIGH
Sum of Estrogens

Cortisol



Flattened slope
Low AUC
(Area Under the Curve)



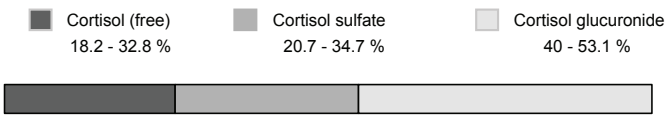
HIGH
Ratio of Cortisol to Testosterone

Cortisol/Testosterone provides insight into relative catabolic (cortisol) and anabolic (testosterone) states.

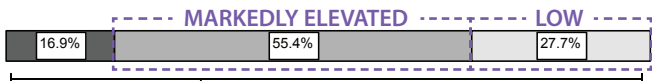
CORTISOL HEAT MAP (HMUS03)

Cortisol Conjugation Pattern

Reference Population (Male)



Patient Result



Cortisol-Cortisone Metabolite Balance

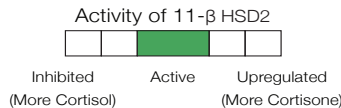


Richard's CHI Results cont.

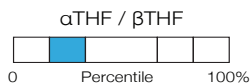
CORTISOL HEAT MAP (HMUS03)

Activity of 11-β HSD2

This marker informs on the nature of the activity of 11-β HSD2 enzyme. 11-β HSD2 converts cortisol to inactive cortisone in kidneys, distal colon and saliva glands. When this enzyme is markedly inhibited free cortisol will be much greater than free cortisone. When the enzyme is upregulated free cortisone will typically be much greater than free cortisol.

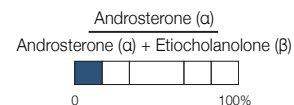


Alpha Reductase Preference



Alpha reductase preference may be influenced by thyroid status.

ANDROGEN-KETOSTEROIDS HEAT MAP (HMUS05)



Clinical Summary

Richard has very low levels of androgens and 17-ketosteroids (DHEA & metabolites) along with significantly elevated estrogens, which suggests aromatase activity is driving the conversion of testosterone to estradiol. Aromatase activity can be driven by cortisol and/or intra-abdominal fat. Indicators of decreased thyroid hormone activity are present including low alpha reductase preference (αTHF/βTHF) and very low Androsterone Excretion Ratio (A/A+E). The high proportion of cortisol sulfate may indicate increased sulfotransferase activity. In this case, a practitioner may speculate that increased sulfotransferase activity for cortisol is also sulfating thyroid hormone, which is known to accelerate thyroid hormone deactivation by deiodinases. Richard has a flattened curve in his Free Cortisol Profile, and the area under the curve (amount of free cortisol in profile) is also low, both of which are consistent with symptoms of fatigue, weakness, and aches and pains. Note that even when Cortisol Metabolites are normal, it is possible to have low free cortisol, and the associated low cortisol symptoms. A high ratio of cortisol to androgens can contribute to loss of muscle mass and aches and pains. Some of Richard's symptoms may also be related to decreased thyroid hormone activity (e.g. constipation).

Possible Clinical Interventions*

- Consider zinc, melatonin, and/or flavonoid supplementation to decrease aromatase activity and conversion of testosterone to estradiol.
- Order confirmatory thyroid studies (serum thyroid stimulating hormone (TSH) or urine thyroid).
- Consider serum sex hormone binding globulin (SHBG) and homeostasis model assessment of insulin resistance (HOMA-IR) to assess for metabolic syndrome and/or insulin resistance (linked to low androgens, high estradiol in men).
- Consider high intensity interval training and/or intermittent fasting to boost testosterone and growth hormone levels, thereby reducing abdominal fat.

The results from CHI provide you with confidence in treatment decision making.

* Interventions are for discussion purposes - CHI does not provide patient-specific treatment recommendations.

CHI Can Benefit Patients like Tamara



Age: 41 year old female

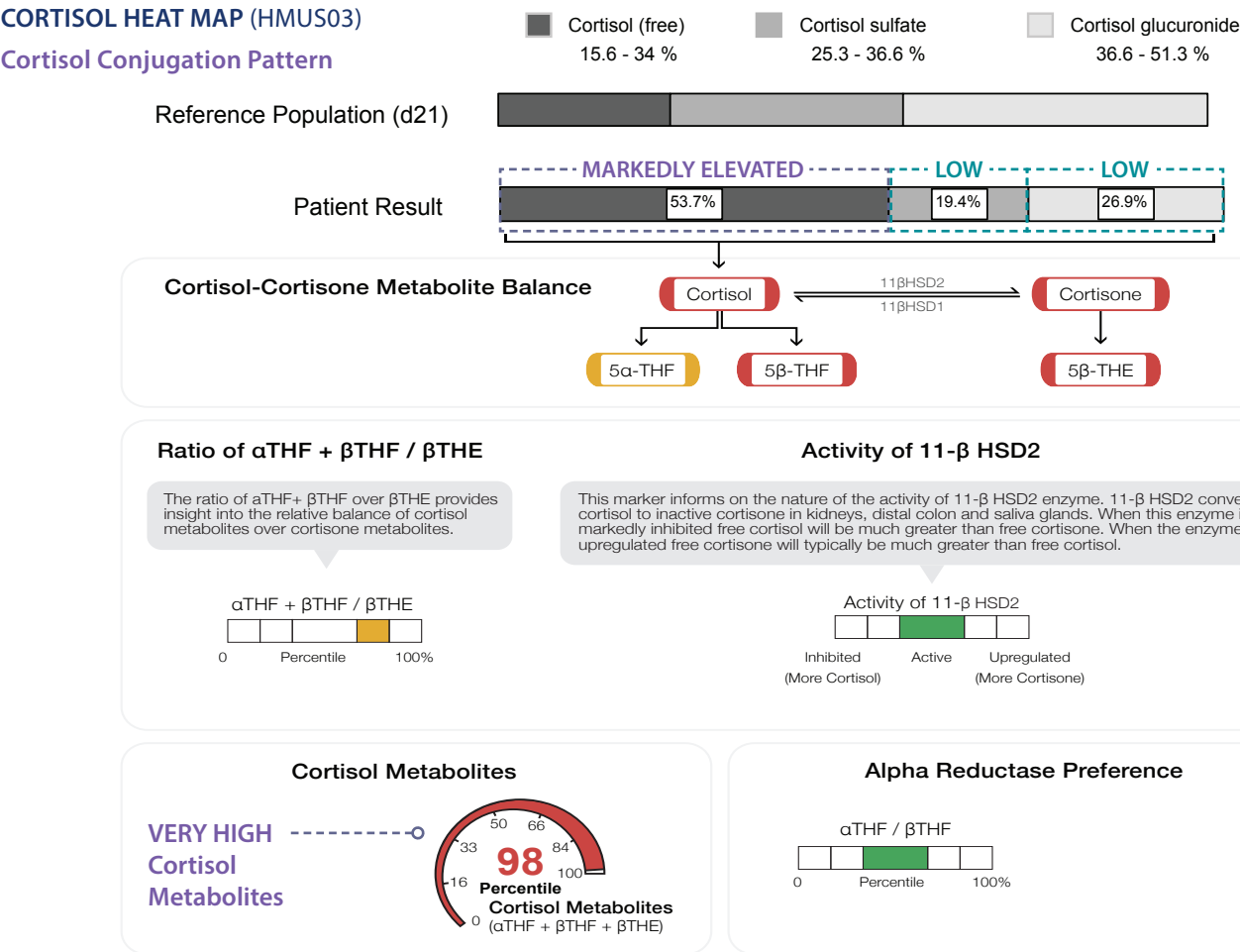
BMI: 21.3 kg/m²

Relevant History: Had her first child ten years ago and began serious fitness training after pregnancy. Non-smoker, healthy diet.

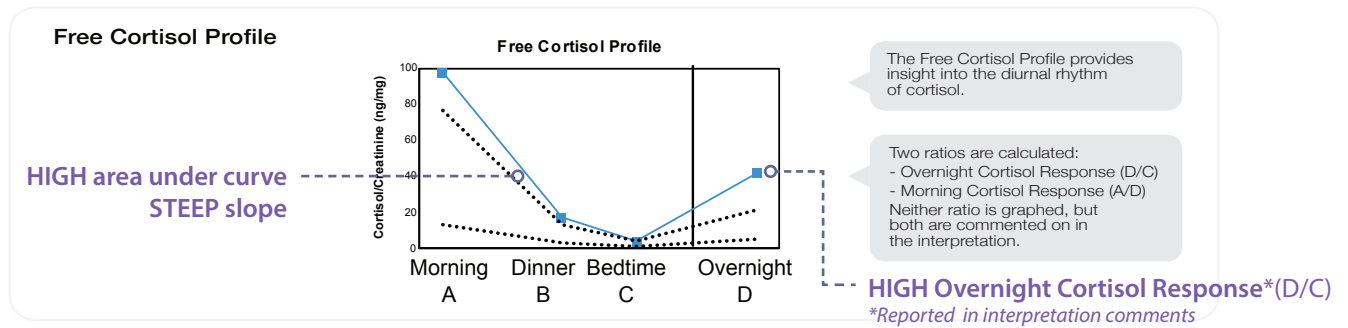
Primary complaints: Tamara presented to her doctor with trouble conceiving, insomnia, foggy thinking, anxiety, and irritability.

Is there an underlying hormone issue at the heart of Tamara's health concerns?

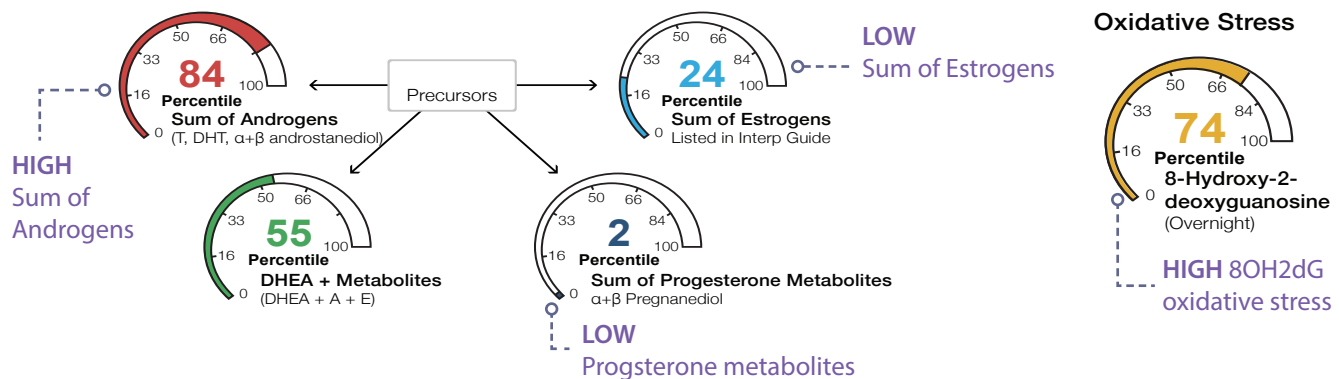
Tamara's CHI Results



Tamara's CHI Results cont.



SUMMARY PAGE (HMUS01)



Clinical Summary

Tamara's BMI is at the low end of normal, and she has a high Sum of Androgens, low Sum of Estrogens, very low Progesterone metabolites and significantly elevated Cortisol Metabolites, all of which may impact her ability to conceive. The steep slope in Tamara's Free Cortisol Profile suggests she is "always on", and her Overnight Cortisol Response suggests the presence of chronic stress, anxiety and/or depression.

Tamara's elevated 8-hydroxy-2-deoxyguanosine (a biomarker of oxidative stress) combined with elevated Cortisol Metabolites, and low proportion of cortisol sulfate suggest the presence of inflammation. Inflammation has been shown to induce the sulfatase enzyme,* that removes the sulfate conjugate and creates more free hormone.

*Research has shown that inflammation induces sulfatase enzymes for DHEA¹⁴, and this is also believed to be true for cortisol (physiologically useful to generate free cortisol in the presence of inflammation).

Possible Clinical Interventions*

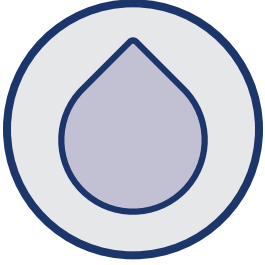
- Curcumin inhibits 11-beta hydroxysteroid dehydrogenase type 1 (11βHSD1) activity, reduces free cortisol, and also has anti-inflammatory effects.
- Phytoestrogens may help with low estrogen symptoms.
- Phosphatidylserine may help reduce cortisol.
- Low dose progesterone cream in luteal phase may be beneficial.

CHI provides you with **clinically relevant information** about your patient's condition.

* Interventions are for discussion purposes - CHI does not provide patient-specific treatment recommendations.

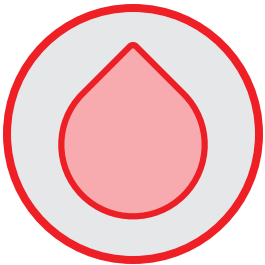
Comparing Hormone Testing Methods

RMA is the only functional medicine laboratory in Canada that offers the top three most common methods of hormone testing: saliva, serum, and urine.



Saliva

- Measures levels of hormones that have passed through tissue (i.e. the salivary gland)
- Provides insight into levels of hormones that are capable of binding to target-tissue receptors
- Is an excellent method for measuring **endogenous** hormone levels
- Measures free hormones and hormones that are loosely bound to albumin
- Reflects exposure to supplemented hormones, and may reflect stored hormones
 - This may be useful for troubleshooting hormone therapy, particularly topical hormones



Serum

- Serum tends to underestimate the amount of hormone present when topically applied hormones are used
 - Most useful for measuring **endogenous** hormone levels
 - Serum hormone levels are not reflective of the clinical effects of hormone skin creams
- A limited menu of hormones and metabolites are tested in serum



Urine

- Provides a view into overall production of each hormone category (estrogens, androgens, progesterone, glucocorticoids) through the measurement of the metabolites
- Useful for determining how the body metabolizes supplemented hormones, particularly estrogens, testosterone, and cortisol
- Provides a view into hormone conjugation, which may be affected by liver function, availability of conjugates and genetic polymorphisms that impact the ability to conjugate
- Like serum testing, urine may under-represent topically applied hormones.
- Urine may over-represent orally supplemented hormones as they are rapidly converted to conjugates

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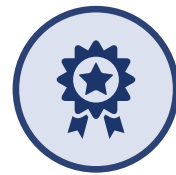
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