DUTCH FEST 2026 | WORKBOOK

2026

DALLAS, TX • MARCH 12-14

dutch Fest

Workbook

PRECISION ANALYTICAL INC.
CREATORS OF THE DUTCHTEST®

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Welcome

A Note from Our Founder

On behalf of the entire Precision Analytical team, thank you for joining us this weekend for DUTCH Fest!

I want to express my gratitude for your decision to be here. As healthcare providers, you dedicate your lives to caring for others, often with demanding schedules and ever-growing responsibilities. Your willingness to invest time in learning, refining your clinical skills, and deepening your understanding of the DUTCH Test speaks volumes about your commitment to delivering meaningful care to your patients.

When I first developed the DUTCH Test, my vision was simple but ambitious: to equip providers with clearer, more actionable insights that could truly improve patient outcomes. Seeing the ways many of you have integrated DUTCH testing into your practices and the impact that has followed continues to inspire the entire DUTCH team!

Over the next two days, my hope is that this experience strengthens your confidence, sharpens your interpretive skills, and provides practical tools you can immediately apply in clinical settings. Through case studies, foundational principles, and expert-led sessions, we aim to create an environment that is not only educational, but collaborative and engaging.

DUTCH Fest is also about community. It's an opportunity to connect with peers, exchange ideas, ask questions, and learn from one another. Some of the most valuable insights often come from shared experiences and conversations, and I encourage you to fully engage in those moments.

Thank you for your trust, your curiosity, and the care you bring to your work every day. It's a privilege to support the important role you play in improving patients' lives.

I'm honored you are here and excited for the days ahead!

Thank you for trusting us to be part of your practice.

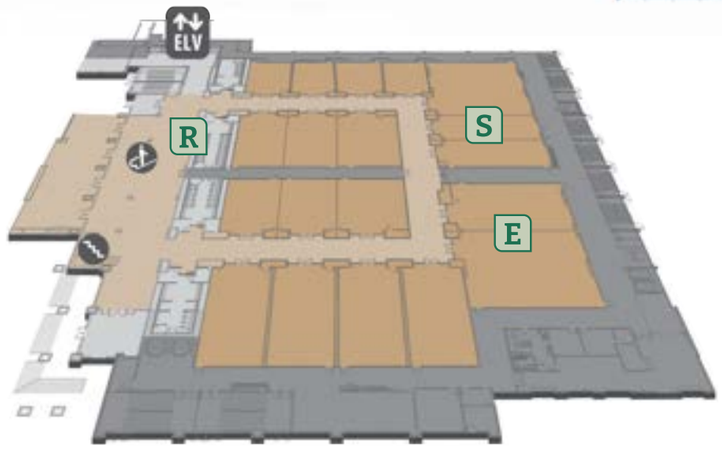
Mark Newman, MS

Founder & CEO of Precision Analytical

Welcome

GAYLORD TEXAN RESORT | OVERVIEW

VINEYARD TOWER | LEVEL 1



COLOR LEGEND

- Lone Star Tower
- Hill Country Atrium
- Riverwalk Atrium
- Vineyard Tower
- Convention Center
- Property Grounds

KEY

- Concierge
- Front Desk
- Valet
- Resort Transportation
- Car Rental
- Restrooms
- Elevator
- Stairs
- Escalator
- Bell Services

GLASS CACTUS SHUTTLE

Join us Saturday night at the Glass Cactus! Kick up your heels at the Glass Cactus, the exclusive waterfront nightlife venue at the Gaylord for food, live music, and dancing. A shuttle will be provided, locate the pick-up/drop-off location on the map:

- Glass Cactus Nightclub Shuttle

Address: 1501 Gaylord Trail, Grapevine, TX 76051

DUTCH FEST NAVIGATION

We will be primarily in the vineyard tower on level 1 for the duration of DUTCH Fest. Below is a key for the main locations we will reference:

- R Registration
- S Sessions (High Plains Room)
- E Exhibit Hall (Mesilla Room)

SCHEDULE

MAR 12

4:00 – 7:00 PM	**Registration**
6:00 – 9:30 PM	**Welcome Party** *Texan Station Bar & Grill (Gaylord Lobby)*

MAR 13

6:00 – 7:00 AM	**Morning Meet-Up**
7:00 AM	**Registration Open**
7:00 – 8:00 AM	**Breakfast** *Exhibitor Hall*
8:00 AM – 1:00 PM	**Morning Sessions**
1:00 – 2:00 PM	**Lunch** *Exhibitor Hall*
2:00 – 5:00 PM	**Case Study Sessions**
7:00 – 9:30 PM	**Live Music & Dinner** *Glass Cactus*

MAR 14

6:00 – 7:00 AM	**Morning Meet-Up**
7:00 – 8:00 AM	**Breakfast** *Exhibitor Hall*
8:00 AM – 1:00 PM	**Morning Sessions**
1:00 – 2:00 PM	**Lunch** *Exhibitor Hall*
2:00 – 5:00 PM	**Case Study Sessions**

DOWNLOAD THE HOTEL MAP

You can also download the **Gaylord Hotels App** for step-by-step directions to find your room, meeting, and resort amenities.

THE SPEAKERS

MARK NEWMAN, MS

Founder and President of Precision Analytical, Inc., is the innovative mind behind the DUTCH Test and a leader in advancing hormone testing through rigorous science and data.

CARRIE JONES, ND

Internationally recognized speaker and educator on the topic of women's health and hormones. Dubbed the "Queen of Hormones," she has advanced training in endocrinology and led medical education at Rupa Health. She now consults across the women's health space, hosts the Hello Hormones podcast, and serves as Chief Medical Officer at NuEthix Formulations.

JACLYN SMEATON, ND

Renowned naturopathic physician and Chief Medical Officer at Precision Analytical, is celebrated for her clinical expertise in fertility, women's health, and integrative endocrinology.

THE AGENDA

DAY 1 | MARCH 12

REGISTRATION OPENS

4:00 – 9:00 PM *Vineyard Tower Lobby*

Welcome to DUTCH Fest 2026 at the Gaylord Texan! Our registration desk will be located in the Vineyard Tower Lobby, located to the right of the main Gaylord Texan hotel check-in. At registration, our team will provide you with your badge, lanyard, event schedules, and more. After you've registered, please join us at the *DUTCH Fest Welcome Party* from 6:00 - 9:30 PM at the Texan Station Bar & Grill.

DUTCH FEST 2026 WELCOME PARTY!

6:00 – 9:30 PM *Texan Station Bar & Grill (Gaylord Lobby)*

DUTCH Fest 2026 Welcome Party! Join us for free drinks, appetizers, and DUTCH-themed trivia at the Texan Station Bar & Grill, located off the Gaylord Texan main lobby. Meet fellow functional health practitioners, learn about DUTCH plus other exhibitors, and get ready to learn all you can in the days ahead.

Trivia will be from 7:30 - 8:30 PM.

DAY 2 | MARCH 13

MORNING MEET-UP OPTIONS

6:00 – 7:00 AM

Pick from the below! *Relâche Fitness Center OR Starbucks on the Veranda*

- **Gym:** Join DUTCH Clinical Educator Dr. Tim Hyatt, ND at the Relâche Fitness Center for an informal warm-up and exercise session.
- **Coffee:** Join members of the DUTCH Clinical Team at Starbucks on the veranda of the Alamo, located in the Gaylord Atrium. Come with questions!

BREAKFAST

7:00 – 8:00 AM *Exhibitor Hall*

Breakfast in Mesilla Exhibitor Hall | Mingle with DUTCH Fest exhibitors while you start your day with food built to power your body and brain for the hours ahead.

REGISTRATION OPEN

7:00 AM - 5:00 PM *Vineyard Tower Lobby*

Check in for Day 2 | DUTCH Fest Registration Desk will be located in the Vineyard Tower Lobby. Follow signs located in the Gaylord Texan check-in area. If you have not already picked up your DUTCH Fest gear Thursday evening, be sure to check in first thing. Today's sessions will introduce you to the DUTCH Dozen, a powerful clinical algorithm that supports your interpretation of the DUTCH Complete and the DUTCH Plus. Focusing primarily on the summary page of the report, you will feel comfortable

identifying the most important and impactful insights from the DUTCH Test, including estrogen and progesterone interpretation, androgens and androgen metabolites, and the HPA axis and cortisol function.

OPENING REMARKS: WELCOME TO DUTCH FEST

8:00 – 8:15 AM *Session Hall (High Plains)*

Join Chief Revenue Officer, Noah Reed, as he kicks off the festival. This will be followed by the first session, hosted by DUTCH Founder, Mark Newman, MS.

MASTER DUTCH TEST ESSENTIALS WITH EFFICIENCY & SPEED

8:15 – 9:15 AM **Presented by Mark Newman, MS**

The DUTCH Test was designed to help providers unravel even the most complex hormonal cases. In this exciting DUTCH Fest kickoff, our founder, Mark Newman, will share the why behind cases where DUTCH really makes the difference in hormone understanding. Attendees will be introduced to the "DUTCH Dozen," the 12 key elements of the DUTCH Test, and an interpretation framework that can increase confidence and efficiency in interpretation, laying a foundation not only for effective clinical interpretation but also successful integration into your practice.

ESTROGEN & PROGESTERONE INTERPRETATION: ADVANCING YOUR KNOWLEDGE USING THE DUTCH DOZEN

9:25 AM – 10:25 AM **Presented by Jaclyn Smeaton, ND**

This session empowers learners to master their understanding of estrogen and progesterone-related elements of the DUTCH Test. Participants will evaluate estrogen and progesterone production in the context of reproductive status, learning to confirm ovulation and identify signs of estrogen dominance. Additionally, we will evaluate preference for the protective 2-OH pathway in phase 1 estrogen metabolism and assess methylation efficiency in phase 2.

BREAK

10:30 – 10:50 AM *Exhibitor Hall*

Visit the Mesilla Exhibitor Hall to speak with DUTCH Fest exhibitors or grab a refreshment. Restrooms are at either end of the Vineyard Tower Lobby.

ANDROGEN INTERPRETATION: DEVELOPING PROFICIENCY USING THE DUTCH DOZEN

11:00 – 11:50 AM **Presented by Jaclyn Smeaton, ND**

This session equips DUTCH providers with the skills to master the androgen-related elements of the DUTCH Test. Participants will evaluate Total DHEA production, assess its influence on downstream metabolites, and identify if testosterone levels could be contributing to patient complaints. Additionally, we will explore 5a-androstanediol as a marker of intracellular 5a-DHT activity and analyze the preference for 5a-metabolism to evaluate its impact on androgen activity.

CORTISOL INTERPRETATION: BUILDING YOUR EXPERTISE IN HPA AXIS INTERPRETATION USING THE DUTCH DOZEN

12:00 – 12:50 PM **Presented by Carrie Jones, ND**

This talk focuses on the four cortisol-related elements of the DUTCH Test, equipping learners to assess HPA axis function comprehensively. Participants will evaluate the daily free cortisol pattern and its impact on sleep, energy, and more. Additionally, participants will analyze the 24-hour free cortisol, metabolized cortisol, and cortisol clearance rate to further gain precise insights into their patients' HPA axis health.

LUNCH BREAK

1:00 – 2:00 PM *Exhibitor Hall*

Get your fill of nutritious foods in the Mesilla Exhibitor Hall while visiting with DUTCH Fest exhibitors. This will be a grab-go, mingle and munch hour between talks.

WHITEBOARD INTERPRETATION WORKSHOP

2:05 – 2:30 PM **Presented by Mark Newman, MS**

Sharpen your clinical skills in this hands-on workshop focused on interpreting DUTCH Test reports. Participants will practice identifying common hormone patterns and collaborate with their teams to accurately match report findings with realistic patient profiles. This session emphasizes practical application, pattern recognition, and clinical decision-making.

CASE STUDY 1: BURNOUT (42-YEAR-OLD FEMALE)

2:30 – 3:00 PM **Presented by Jaclyn Smeaton, ND & Mark Newman, MS**

Meet Teresa: Depressed, low exercise tolerance, joint pain everywhere, diagnosed with Rheumatoid Arthritis, drinking to cope. Her cortisol is flat-lined, sex hormones tanked, and methylation is slow. This is stage 3 HPA axis dysfunction in real time — can we help get her energy and spirits up?

CASE STUDY 2: MENOPAUSE (51-YEAR-OLD FEMALE)

3:00 – 3:30 PM **Presented by Jaclyn Smeaton, ND & Mark Newman, MS**

Meet Emma: One-year post-menopause: nightly hot flashes, insomnia, creeping weight gain, painful sex, and recurrent UTIs. Labs show low estrogen/progesterone and sky-high bedtime cortisol sabotaging her sleep. Can we help fix her sleep, flashes, and metabolism all at once?

BREAK

3:30 – 4:00 PM *Exhibitor Hall*

Visit the Mesilla Exhibitor Hall to speak with DUTCH Fest exhibitors or grab a refreshment. Restrooms are at either end of the Vineyard Tower Lobby.

CASE STUDY 3: ACNE (35-YEAR-OLD FEMALE)

4:00 – 4:30 PM **Presented by Carrie Jones, ND & Mark Newman, MS**

Meet Jenna: Cystic acne, bloating, anxiety, and depression. Total testosterone normal… but she's shunting everything down the potent 5α-reductase pathway resulting in high 5α-DHT driving her breakouts. Add in a genotoxic 4-OH estrogen preference and strong family history of breast cancer. Can we improve her acne and then more?

CASE STUDY 4: INFERTILITY & PCOS (31-YEAR-OLD FEMALE)

4:30 – 5:00 PM **Presented by Carrie Jones, ND & Mark Newman, MS**

Meet Gabby: Difficulty conceiving, losing hair, adult acne, and chronically stressed. She's overweight, insulin-resistant, anovulatory with high baseline estrogen (think about endometrial hyperplasia risk!) Fix the root cause or keep giving Clomid?

CLOSING REMARKS: DAY ONE

5:00 – 5:15 PM *Session Hall (High Plains)*

Closing remarks plus a look ahead at DUTCH Fest, Day Two! Hosted by DUTCH Founder, Mark Newman.

LIVE MUSIC & DINNER

7:00 – 9:30 PM *Glass Cactus*

Join us at the Glass Cactus! Kick up your heels at the Glass Cactus, the exclusive waterfront nightlife venue at the Gaylord. There will be free drinks & dinner with live music and line dancing from The Grooves. Free shuttle service departs from the Gaylord Texan valet station starting at 6:45 PM. The Glass Cactus is located on Gaylord grounds, but is approximately 0.3 miles down the entrance road.

DAY 3 | MARCH 14

MORNING MEET-UP OPTIONS

6:00 – 7:00 AM

Pick from the below! *Relâche Fitness Center OR Starbucks on the Veranda*

- **Gym:** Join DUTCH Clinical Educator, Dr. Tim Hyatt, ND, at the Relâche Fitness Center for an informal warm-up and exercise session.
- **Coffee:** Get to know DUTCH Founder, Mark Newman! Come with questions about the origin and the future of DUTCH testing. This will be at Starbucks on the veranda of the Alamo, located in the Gaylord Atrium.

BREAKFAST

7:00 – 8:00 AM *Exhibitor Hall*

Breakfast in Mesilla Exhibitor Hall | Mingle with DUTCH Fest exhibitors while you start your day with food built to power your body and brain for the hours ahead.

REGISTRATION OPEN

7:00 AM - 8:00 AM *Vineyard Tower Lobby*

Check in for Day 3 | Today's sessions will go beyond the DUTCH interpretation basics and focus in on more than a dozen advanced patterns and insights, which can be assessed with the DUTCH Test. Learn how to leverage every data point on the report to hone your clinical assessment and create a thorough treatment plan. The DUTCH Fest Registration Desk will be located in the Vineyard Tower Lobby. Follow signs located in the Gaylord Texan check-in area.

OPENING REMARKS: DAY THREE

8:00 – 8:15 AM *Session Hall (High Plains)*

Join Chief Revenue Officer, Noah Reed, as he kicks off DUTCH Fest Day Three. This will be followed by the first session hosted by DUTCH Founder, Mark Newman, MS.

RECOGNIZING ADVANCED PATTERNS WITH DUTCH

8:15 – 9:15 AM **Presented by Mark Newman, MS**

This talk inspires learners to become DUTCH interpretation experts, highlighting how mastery can revolutionize patient treatment plans. Participants will familiarize themselves with the advanced concepts within the DUTCH Test that go far beyond the fundamentals. By exploring the DUTCH Advanced Insights framework, attendees will learn how to leverage the tools to elevate their interpretation skills and deliver the most impactful, personalized care.

ESTROGEN & PROGESTERONE INTERPRETATION: EXCELLING IN YOUR INTERPRETATION USING DUTCH ADVANCED INSIGHTS

9:25 – 10:25 AM **Presented by Jaclyn Smeaton, ND**

This talk delves into the four estrogen and progesterone-related DUTCH concepts, providing an understanding of their deeper clinical applications. Learners will evaluate E1, E3, and Total Estrogen levels to assess estrogen activity, analyze progesterone's 5a-metabolism for its calming GABA effects, and examine estrogen clearance efficiency through phases 1 and 2. Additionally, participants will identify abnormalities in related organic acids, such as MMA and melatonin, and uncover their relevance to estrogen and progesterone imbalances.

BREAK

10:30 – 10:50 AM *Exhibitor Hall*

Visit the Mesilla Exhibitor Hall to speak with DUTCH Fest exhibitors or grab a refreshment. Restrooms are at either end of the Vineyard Tower Lobby.

ANDROGEN INTERPRETATION: MASTERING THE SCIENCE USING THE DUTCH ADVANCED INSIGHTS

11:00 – 11:50 AM **Presented by Carrie Jones, ND**

This talk explores the advanced concepts necessary for the deepest understanding of androgen-related DUTCH insights. Participants will evaluate the balance between DHEA-S and Total DHEA, considering its possible link to inflammation, and assess whether urine testosterone accurately reflects systemic levels, accounting for the UGT2B17 deletion. Attendees will also confirm cellular androgen activity via 5a-DHT and identify abnormalities in androgen-related organic acids.

CORTISOL INTERPRETATION: BECOMING A CLINICAL EXPERT IN THE EVALUATION OF HPA AXIS HEALTH USING THE DUTCH ADVANCED INSIGHTS

12:00 – 12:50 PM **Presented by Carrie Jones, ND**

This talk focuses on the advanced cortisol-related DUTCH concepts, enabling learners to refine and master their HPA axis assessment skills. Participants will understand free cortisone's role in enhancing cortisol interpretation, evaluate the body's preference for active cortisol versus inactive cortisone using THF and THE markers, and learn to identify anabolic versus catabolic states. Participants will learn to identify abnormalities in cortisol-related organic acids, such as melatonin and vanilmandelate (VMA), and understand their relevance to cortisol imbalances.

LUNCH BREAK

1:00 – 2:00 PM *Exhibitor Hall*

Get your fill of nutritious foods in the Mesilla Exhibitor Hall while visiting with DUTCH Fest exhibitors. This will be a grab-go, mingle and munch hour between talks.

WHITEBOARD INTERPRETATION WORKSHOP

2:05 – 2:30 PM **Presented by Mark Newman, MS**

Sharpen your clinical skills in this hands-on workshop focused on interpreting DUTCH Test reports. Participants will practice identifying common hormone patterns and collaborate with their teams to accurately match report findings with realistic patient profiles. This session emphasizes practical application, pattern recognition, and clinical decision-making.

CASE STUDY 5: ENDOMETRIOSIS & DYSMENORRHEA (20-YEAR-OLD FEMALE)

2:30 – 3:00 PM **Presented by Jaclyn Smeaton, ND & Mark Newman, MS**

Meet Anna: New high-pressure job, crippling period pain, endometriosis, heavy bleeding, headaches, and terrible sleep. Elevated high-sensitivity CRP and borderline-high sex hormones (i.e., testosterone and estrogen) are contributing to her picture. Can we help calm the fire and get her feeling good again?

CASE STUDY 6: AMENORRHEA (29-YEAR-OLD FEMALE)

3:00 – 3:30 PM **Presented by Jaclyn Smeaton, ND & Mark Newman, MS**

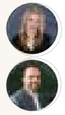
Meet Tanya: Underweight, diagnosed with an eating disorder, hypothyroid, no periods, hot flashes, and crippling anxiety. Her estrogen and progesterone are below the postmenopausal range, yet her cortisol is very high. A case of hypothalamic amenorrhea and relative energy deficiency — can we get her ovulating again?

BREAK

3:30 – 4:00 PM *Exhibitor Hall*

Visit the Mesilla Exhibitor Hall to speak with DUTCH Fest exhibitors or grab a refreshment. Restrooms are at either end of the Vineyard Tower Lobby.

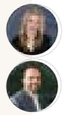
CASE STUDY 7: EARLY PERIMENOPAUSE (47-YEAR-OLD FEMALE)



4:00 – 4:30 PM **Presented by Carrie Jones, ND & Mark Newman, MS**

Meet Shreya: Cycles irregular at 11–21 days, heavy bleeding, breast pain, night wakings, crushing fatigue, and iron-deficiency anemia — all while her estrogen is above range and she's rarely ovulating. Classic early-stage perimenopause ovarian dysfunction. Can we help her feel like herself again?

CASE STUDY 8: SEXUAL DYSFUNCTION (49-YEAR-OLD MALE)



4:30 – 5:00 PM **Presented by Carrie Jones, ND & Mark Newman, MS**

Meet Rob: Erectile dysfunction, can't build muscle, exhausted, depressed, and gaining weight despite trying. He struggles with obesity, fatty liver, hypertension, high cholesterol, and prediabetes. Labs reveal low testosterone but high estrogen - classic late-onset male hypogonadism driven by metabolic dysfunction. Can we help him feel young(er) again?

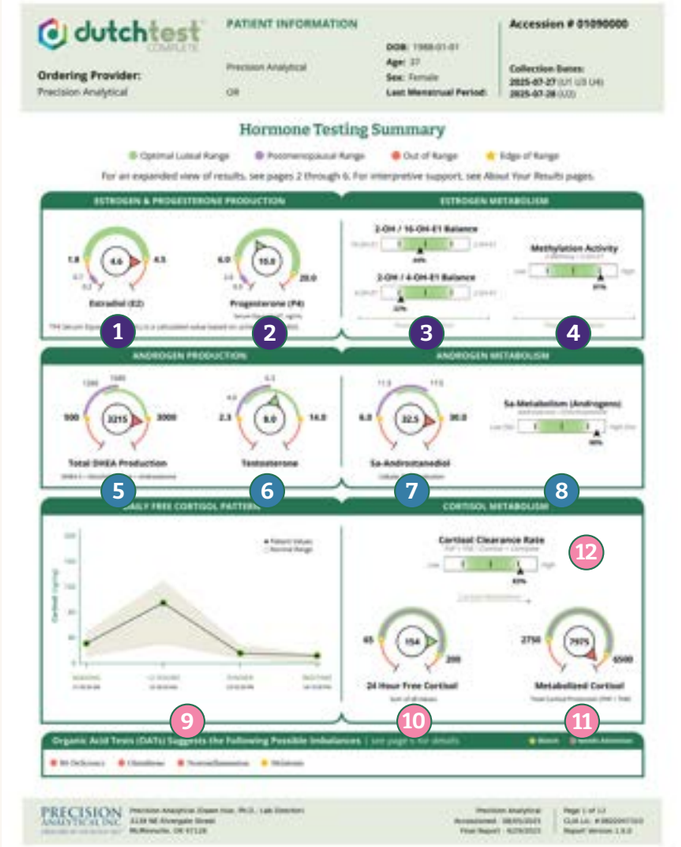
CLOSING REMARKS

5:00 – 5:15 PM *Session Hall (High Plains)*

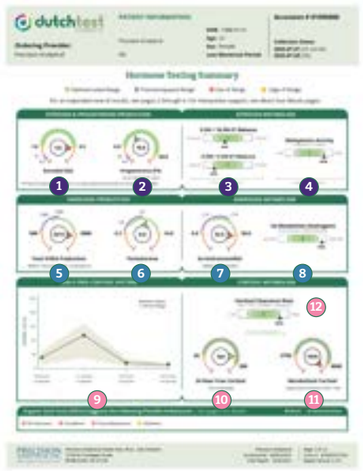
Presented by DUTCH Founder, Mark Newman | Thank you for joining us at DUTCH Fest and for the commitment you show every day to advancing patient care. Your willingness to invest in learning, collaboration, and clinical growth is what drives innovation and meaningful outcomes in this field. It's truly an honor to be part of such a dedicated community.

THE DUTCH DOZEN
FEMALE

The DUTCH Dozen is an interpretive framework that allows clinicians to understand their patients' DUTCH Test results quickly and comprehensively. We have streamlined the review of the DUTCH Test with a set of 12 assessments that prioritize the most critical aspects of hormone function, covering estrogens, progesterone, androgens, and cortisol. The DUTCH Dozen allows clinicians to quickly evaluate key hormone markers in the **Hormone Testing Summary using page 1 of the report**, making it easier and faster to develop targeted treatment plans. For best practice, start with the DUTCH Dozen, then explore details on pages 2, 4, and 6 as needed. For deeper insights, refer to the **DUTCH Advanced Insights** section on page 23.



- Estrogen & Progesterone
- Androgens
- Cortisol



ESTROGEN & PROGESTERONE

1 Assess estrogen levels given the patient's reproductive status

Are estrogen levels normal? **Estradiol (E2)** is the most potent estrogen and thus has more estrogenic activity in the body compared to E1, E3, and the phase 1 and 2 estrogen metabolites. In the example, the premenopausal patient's Estradiol (E2) is above the luteal range at 4.6 ng/mg and could result in symptoms of estrogen excess.

See page 96 and 118 of the DUTCH Interpretive Guide to learn more about estradiol levels for premenopausal and postmenopausal females, respectively. See pages 10-15 of the DUTCH Treatment Guide for treatment considerations relating to estradiol.

2 Assess progesterone levels given the patient's reproductive status

Are progesterone levels normal? Adequate **Progesterone (P4)** is important for opposing estrogen's proliferative effects, among many other things. In the example, the premenopausal patient's Progesterone (P4) Serum Equivalent is within the luteal rang at 10 ng/mL. Ovulation occurred but progesterone levels may not be adequate enough to oppose the high estrogen levels.

See page 102 and 123 of the DUTCH Interpretive Guide to learn more about progesterone levels for premenopausal and postmenopausal females, respectively. See pages 8-9 of the DUTCH Treatment Guide for treatment considerations relating to progesterone.

For cycling females in the luteal phase, the **Estradiol (E2)** and **Progesterone (P4) Serum Equivalent** dials can be easily compared to assess relative balance. In the example, there is an estrogen dominance pattern as the Estradiol (E2) dial is pointing relatively higher than the Progesterone (P4) Serum Equivalent dial.

See page 98 and 120 of the DUTCH Interpretive Guide to learn more about estrogen dominance patterns for premenopausal and postmenopausal females, respectively.

3 Assess 2-OH preference in phase 1 estrogen metabolism

Is the protective 2-OH pathway preferred? The **2-OH estrogen metabolites** are more stable than the other phase 1 estrogen metabolites (16-OH and 4-OH); therefore, a 2-OH preference is favorable.

See page 152 of the DUTCH Interpretive Guide to learn more about 2-OH and see page 30 of the DUTCH Treatment Guide for treatment considerations relating to 2-OH.

2-OH/16-OH-E1 Balance Slider

16-OH is an estrogenic phase 1 metabolite that can potentially worsen estrogen excess associated symptoms and conditions. The **2-OH/16-OH-E1 Balance** slider shows 2-OH-E1 relative to 16-OHE1. As the arrow moves to the left side of the slider, more 16-OH is present relative to 2-OH. In the example, the patient's result is within range at the 44th percentile. This result is favorable as she has high estradiol, and a 16-OH preference would further add to the estrogenic activity in the body.

See page 153 of the DUTCH Interpretive Guide to learn more about 16-OH and see page 29 of the DUTCH Treatment Guide for treatment considerations relating to a 16-OH preference.

2-OH/4-OH-E1 Balance Slider

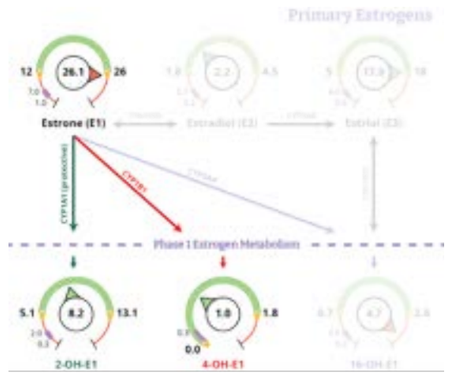
4-OH is a genotoxic metabolite that has been shown to cause DNA damage and increase risk for breast cancer. The **2-OH/4-OH-E1 Balance** slider shows 2-OH-E1 relative to 4-OH-E1. As the arrow moves to the left side of the slider, more 4-OH is present relative to 2-OH. In the example, the patient's result is within range but at the low end at the 22nd percentile, indicating a 4-OH preference (only 22% of people favor the 4-OH pathway more than they do). This result is not favorable, especially because her 4-OH-E1 and 4-OH-E2 are elevated (in subsequent pages of the report). For the majority of people, it may be less ideal when this percentage is on the low end or below range (low end is <20%-30%; below range is ≤20%).

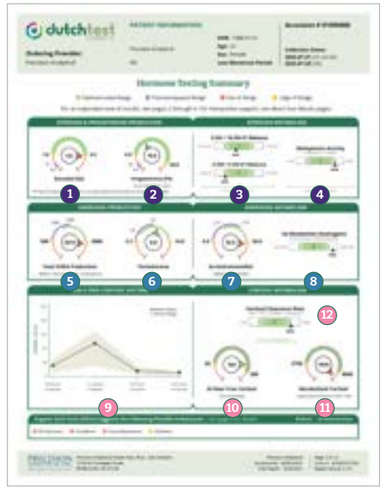
See page 152 of the DUTCH Interpretive Guide to learn more about 4-OH and see page 28 of the DUTCH Treatment Guide for treatment considerations relating to a 4-OH preference.

4 Assess methylation of 2-OH estrogens

Are 2-OH estrogens being adequately methylated? The majority of 2-OH and 4-OH estrogens are methylated in phase 2 of estrogen detoxification. The **Methylation Activity** slider bar shows the ratio 2-Methoxy/2-OH-E1. 2-Methoxy-E1 is a neutral, stable phase 2 metabolite that is easily excreted from the body. The patient's result is shown by the black arrow. When results are to the left it indicates lower than average methylation activity, to the right indicates higher than average activity. In the example, the patient's result is at the 81st percentile, indicating significantly high methylation activity (81% of people have slower methylation than they do). This result is favorable, especially with high E1, and E2 levels. For the majority of people, it may be less ideal when this percentage is on the low end or below range (low end is <20%-30%; below range is ≤20%) however, 2-OH, 4-OH, E1, and E2 values also need to be considered. For example, if 2-OH, 4-OH, E1 and E2 are above range, it may be more beneficial for the methylation activity to be >30%.

See page 154 of the DUTCH Interpretive Guide to learn more about 2-Methoxy-E1 and phase 2 methylation and see page 30 of the DUTCH Treatment Guide for treatment considerations relating to methylation.





ANDROGENS

5 Assess adrenal androgen levels (Total DHEA)

Are adrenal androgen levels normal? **Total DHEA Production** is the sum of three urinary DHEA metabolites (DHEA-S, etiocholanolone, and androsterone) and shows the total androgen production from the adrenal glands. In the example, the premenopausal patient's Total DHEA Production is above the premenopausal range at 3,215 ng/mg and could result in symptoms of androgen excess.

See page 109 and 130 of the DUTCH Interpretive Guide to learn more about DHEA levels for premenopausal and postmenopausal females, respectively. See pages 22-24 of the DUTCH Treatment Guide for treatment considerations relating to DHEA.

6 Assess testosterone levels

Are testosterone levels normal? **Testosterone** on the DUTCH Test reflects the bioavailable conjugated testosterone excreted in urine. For most patients, this result will parallel serum free testosterone. In the example, the premenopausal patient's testosterone is within the premenopausal range at 8.0 ng/mg.

See page 106 and 126 of the DUTCH Interpretive Guide to learn more about testosterone levels for premenopausal and postmenopausal females, respectively. See pages 16-17 and 20-21 of the DUTCH Treatment Guide for treatment considerations relating to testosterone.

NOTE

> *If urinary testosterone is below range, confirm low testosterone levels in the serum before considering treatment. This is because a genetic deletion polymorphism (UGT2B17) in some patients may cause very low levels of testosterone in urine while levels may be normal (or high) in serum. See page 72 of the DUTCH Interpretive Guide to learn more. The UGT2B17 deletion will be covered on day 3 of DUTCH Fest.*

7 Assess cellular production of 5a-DHT via 5a-androstanediol

Is cellular production and activity of 5a-DHT normal? 5a-DHT is the most potent androgen and has 4x more androgenic activity than testosterone. **5a-Androstanediol** is a metabolite of 5a-DHT, and research shows that 5a-androstanediol best reflects intracellular production and activity of 5a-DHT. In the example, the premenopausal patient's 5a-androstanediol is above the premenopausal range at 32.5 ng/mg and could result in symptoms of androgen excess.

See page 111 and 132 of the DUTCH Interpretive Guide to learn more about androgen metabolism for premenopausal and postmenopausal females, respectively. See page 25 of the DUTCH Treatment Guide for treatment considerations relating to androgen metabolism (5a/5b Preference).

8 Assess if there is a preference for the more potent alpha metabolism of the androgens

Is there a preference for 5a-reductase metabolism of the androgens? **The 5a-Metabolism (Androgens)** slider shows the Androsterone (5a) / Etiocholanolone (5b) ratio. Results on the left indicate relatively more inactive 5b metabolites. Results to the right indicate more active 5a metabolites, which typically indicates a higher potential for high androgen symptoms. In the example, the premenopausal patient's result is on the high end at the 90th percentile, indicating an alpha preference (90% of people favor the beta pathway more than she does). In this case, the alpha preference is not favorable because 5a-androstanediol is elevated and could result in symptoms of androgen excess. There is no ideal percentile for this slider as androgen levels and symptoms vary. For example, an alpha preference in the absence of high androgen levels and androgen-excess symptoms may not need addressing.

See page 111 and 132 of the DUTCH Interpretive Guide to learn more about androgen metabolism for premenopausal and postmenopausal females, respectively. See page 25 of the DUTCH Treatment Guide for treatment considerations relating to androgen metabolism (5a/5b Preference).

CORTISOL

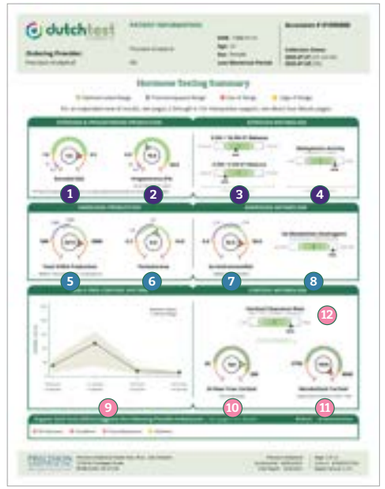
9 Assess the daily free cortisol pattern

Is the daily free cortisol pattern optimal? The **Daily Free Cortisol Pattern** plots free cortisol measured from the individual urine samples taken throughout the day. The reference range is shown in the shaded area behind the patient's results, which are shown by the dark line. The first value reported (WAKING) represents the overnight period. The second value (+2 HOURS) is the peak. Urine samples reflect cortisol levels in the hours before the sample was collected. Saliva samples (on a DUTCH Plus or DUTCH CAR report – not pictured here) reflect cortisol levels at that moment in time. In the example, the patient has a diurnal pattern to their cortisol, and all points are within range. This result is favorable.

See page 160 of the DUTCH Interpretive Guide to learn more about evaluating cortisol. See pages 34, 36-37, 60-62, and 63 of the DUTCH Treatment Guide for general HPA axis support considerations, an herbal support overview, sleep and circadian rhythm support considerations, and stress and parasympathetic activity support considerations, respectively.

10 Assess the daily total of free cortisol in circulation (24hr Free Cortisol)

What is the daily total of free cortisol in circulation? The **24hr Free Cortisol** dial shows the sum of the 4 points on the **Daily Free Cortisol Pattern**. This dial shows overall cortisol exposure throughout the day. In the example, the 24hr Free Cortisol is within range at 154 ng/mg. This result is favorable.



See page 162 of the DUTCH Interpretive Guide to learn more about total free cortisol. See pages 38 of the DUTCH Treatment Guide for treatment considerations relating to total free cortisol.

11 Assess the total cortisol produced by the adrenal glands (Metabolized Cortisol)

What is the total production of cortisol by the adrenals? Cortisol and cortisone are metabolized in the body into a-THF, b-THF, and b-THE. The sum of these equals the **Metabolized Cortisol** and can give insight into total adrenal cortisol production for the day. In the example, the patient's Metabolized Cortisol is above the range at 7,975 ng/mg, signifying high production of cortisol from the adrenals on the day of testing. This result is not favorable.

See page 167 of the DUTCH Interpretive Guide to learn more about metabolized cortisol.

12 Assess the rate of cortisol clearance from the body

Is cortisol being cleared from the body at an appropriate rate? The **Cortisol Clearance Rate (CCR)** is the ratio of THF + THE / Cortisol + Cortisone. This can help assess the rate at which cortisol is cleared from the body. Results on the left indicate slower cortisol clearance, and on the right indicate faster cortisol clearance. A low or high CCR indicates that there is a metabolic component affecting the HPA axis. In the example, the patient's result is at the 82nd percentile, indicating a high (i.e., fast) cortisol clearance rate. This result is not favorable, as it signifies that a hypermetabolic state is affecting the patient's HPA axis. For the majority of people, it is ideal when this percentile is above 20% and below 80%.

See page 168 of the DUTCH Interpretive Guide to learn more about the CCR and see page 39 of the DUTCH Treatment Guide for treatment considerations relating to the CCR.

While the Hormone Testing Summary on page 1 of the DUTCH Test and the DUTCH Dozen provide a comprehensive overview for interpretation, exploring pages 2, 3, 4, and 6 of the DUTCH Test report using the **DUTCH Advanced Insights** may offer additional clarity and a deeper understanding of the results.

ESTROGEN & PROGESTERONE

1 Assess whether E1, E3, and Total Estrogen add more insight into overall estrogenic activity

Do E1, E3, and Total Estrogen add more insight into overall estrogenic activity? E1 is 10% as potent as E2 but is typically more abundant, making it a significant contributor to estrogenic symptoms (high or low). Total Estrogen (listed on the Sex Hormones & Metabolites page) can provide insight into overall estrogen production, however, note that it can be high with robust, healthy estrogen metabolism. E3 is a weak estrogen that may have anti-inflammatory properties, nevertheless, E3 therapy that significantly elevates circulating E3 levels can contribute to estrogenic symptoms in some patients. In the example, the premenopausal patient's E1 and Total Estrogen (not pictured) are above range which confirms high estrogenic activity, and the patient is not using E3 therapy.

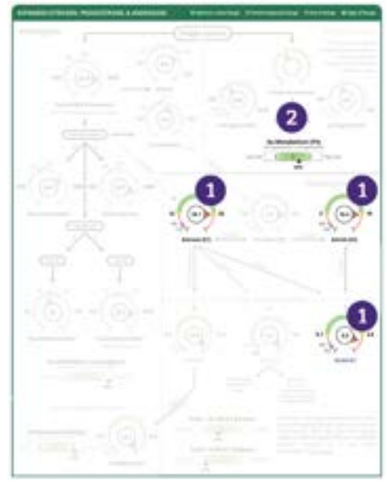
See page 96 and page 118 of the DUTCH Interpretive Guide to learn more about estradiol levels for premenopausal and postmenopausal females, respectively. See pages 10-15 of the DUTCH Treatment Guide for treatment considerations relating to estrogen.

2 Assess if there is a preference for alpha metabolism of progesterone

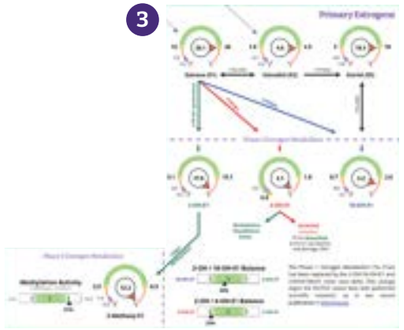
Does progesterone favor alpha metabolism? **The 5a-Metabolism (P4) slider** is the most effective tool for assessing whether progesterone is primarily metabolized through the alpha pathway (into a-pregnanediol) or the beta pathway (into b-pregnanediol). Understanding this preference can be valuable, as alpha progesterone metabolites, such as allopregnanolone and a-pregnanediol, modulate GABA receptors, potentially supporting mood and sleep. While allopregnanolone has significantly stronger sedating effects than a-pregnanediol, internal DUTCH data shows a strong correlation between their levels. In the example, the premenopausal patient's result is within range at the 60th percentile. Note that an alpha (or beta) preference may not always be clinically significant, especially if progesterone levels are low. This concept may be most relevant for patients using oral progesterone.

See page 105 and page 126 of the DUTCH Interpretive Guide to learn more about progesterone metabolism for premenopausal and postmenopausal females, respectively. See pages 8-9 of the DUTCH Treatment Guide for treatment considerations relating to progesterone.

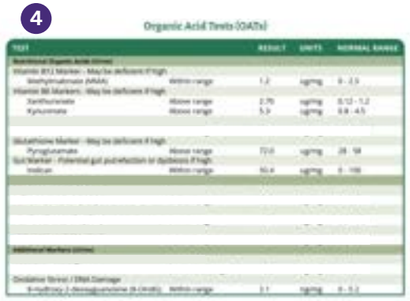
DUTCH ADVANCED INSIGHTS
FEMALE



Page 2 of the report:
Sex Hormones & Metabolites



Page 2 of the report:
Sex Hormones & Metabolites



Page 6 of the report:
Organic Acid Tests (OATs)

3 Assess estrogen clearance through phase 1 and 2

How is estrogen clearance through phase 1 and 2? One can estimate **estrogen clearance** by comparing the phase 1 and 2 metabolites (2-OH, 4-OH, 16-OH, 2-Methoxy-E1) with the primary estrogens (E1 and E2). If the phase 1 and 2 metabolites are much lower compared to the primary estrogens, then the patient may have slow estrogen clearance. If the phase 1 and 2 metabolites are much higher compared to the primary estrogens, then the patient may have fast estrogen clearance. Slow estrogen clearance may put patients at higher risk of estrogen excess conditions. On the contrary, fast estrogen clearance may put patients at a lower risk of estrogen excess conditions. In this example, the phase 1 and 2 estrogen metabolite levels look higher relative to the E1 and E2 levels; thus, the estrogen clearance may be relatively fast, which is favorable especially with high E1 and E2 levels. Note, their phase 2 Methylation Activity is also high at the 81st percentile which is favorable.

4 Assess whether any of the estrogen-related organic acids are out of range

Are any of the estrogen-related organic acids (MMA, Xanthurenate, Kynurenate, Pyroglutamate, Indican, 8-OHdG) above range?

- **Methylmalonate (MMA)** – High MMA may indicate B12 deficiency. B12 supports optimal methylation.
- **Xanthurenate and Kynurenate –** High Xanthurenate and/or Kynurenate may indicate B6 deficiency. B6 supports optimal methylation.
- **Pyroglutamate –** High Pyroglutamate may suggest low glutathione, a key antioxidant that helps protect cells from damage. Low glutathione status is especially significant when the 2-OH/4-OH-E1 Balance slider result is below the optimal range.
- **Indican –** High Indican is a marker of dysbiosis (bacterial imbalance) and intestinal permeability. If paired with high E2 or suboptimal estrogen metabolism, this may contribute to poor estrogen detoxification through the GI tract.
- **8-Hydroxy-2-deoxyguanosine (8-OHdG) –** High 8-OHdG may indicate a higher oxidative stress burden, especially when paired with a high 4-OH-E1 or a low 2-OH/4-OH-E1 ratio.

In the example, the patient's Xanthurenate, Kynurenate, and Pyroglutamate are all high. Glutathione deficiency is especially significant, as the 2-OH/4-OH-E1 Balance slider result is on the low end and 4-OH-E1 and 4-OH-E2 (on page 3 of the report) are above range.

See page 176 of the DUTCH Interpretive Guide to learn more about the Organic Acid Tests (OATs) and see pages 42-47 of the DUTCH Treatment Guide for treatment considerations relating to the OATs.

ANDROGENS

5 Assess if the DHEA-S is relatively lower than the Total DHEA Production

Is **DHEA-S** relatively lower than the **Total DHEA Production** (when each is evaluated against its respective reference range)? When DHEA-S is relatively lower, it may indicate that DHEA is being converted downstream into metabolites like etiocholanolone and androsterone, rather than being sulfated into DHEA-S. Research suggests that low DHEA-S levels in the blood are linked to inflammation, and it is known that inflammation can impair the sulfation process. To assess this, compare the DHEA-S level to the Total DHEA Production. In the example, the patient's DHEA-S level is lower when compared to their Total DHEA Production when each is evaluated against its respective reference range. This may signify inflammation and/or sulfation issues.

See page 190 of the DUTCH Interpretive Guide to learn more about suboptimal sulfation patterns seen on the DUTCH Test. See page 29 of the DUTCH Treatment Guide for treatment considerations relating to suboptimal sulfation.

6 Assess the androgen pattern to determine if urine testosterone may not accurately reflect systemic levels (UGT2B17 deletion)

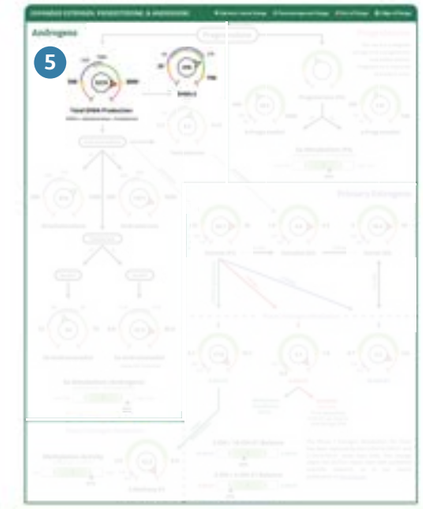
Does the androgen pattern suggest that urine testosterone may not accurately reflect systemic levels? Some people are born with a **genetic deletion polymorphism (UGT2B17)** that causes their testosterone, 5a-DHT, and 5b-androstanediol to be falsely low in the urine but does not affect their 5a-androstanediol or epi-testosterone. For this reason, low and very low urinary testosterone levels should be confirmed with serum testing before treatment. In the example, the androgen pattern does not suggest that urine testosterone may not accurately reflect systemic levels because the testosterone is within range. On the contrary, if the patient had the UGT deletion, their androgen results may look like the top example.

See page 72 of the DUTCH Interpretive Guide to learn more about the UGT deletion.

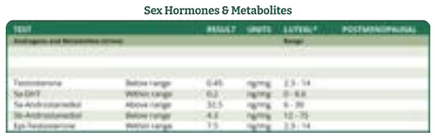
7 While 5a-androstanediol best represents cellular 5a-DHT production, assess if 5a-DHT offers additional insight into androgenic activity

Does 5a-DHT offer additional insight into androgenic activity? **5a-DHT** is the most potent androgen and has 4x more androgenic activity than testosterone. 5a-Androstanediol is a metabolite of 5a-DHT and research shows that 5a-androstanediol best reflects intracellular production and activity of 5a-DHT, but it can also be insightful to look at the actual 5a-DHT result. In the example on the previous page, the patient's 5a-DHT is almost above range at 6.5 ng/mg and confirms high androgen activity.

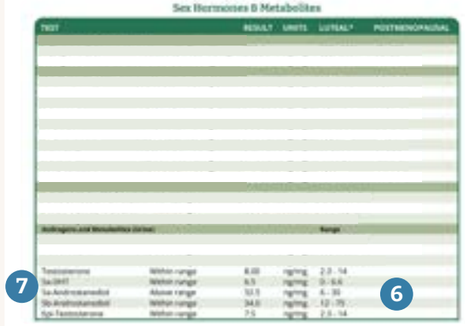
See page 111 and page 132 of the DUTCH Interpretive Guide to learn more about androgen metabolism for premenopausal and postmenopausal females, respectively. See page 25 of



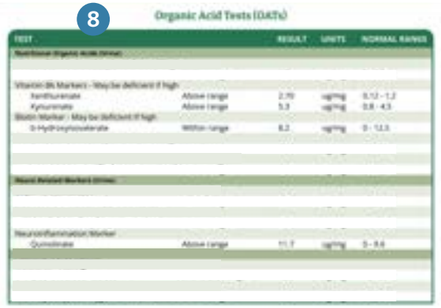
Page 2 of the report:
Sex Hormones & Metabolites



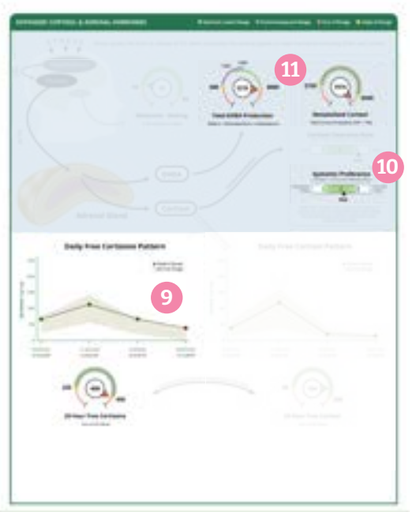
Page 3 of the report:
UGT2B17 Example



Page 3 of the report:
Sex Hormones & Metabolites Data



Page 6 of the report:
Organic Acid Tests (OATs)



Page 4 of the report:
Adrenal Hormones & Metabolites

the DUTCH Treatment Guide for treatment considerations relating to androgen metabolism (5a/5b Preference).

8 Assess whether any of the androgen-related organic acids are out of range

Are any of the androgen-related organic acids (Xanthurenate, Kynurenate, Quinolinate) above range?

- **Xanthurenate and Kynurenate –** High Xanthurenate and/or Kynurenate may indicate abnormalities in tryptophan metabolism. Abnormalities in tryptophan metabolism have been linked to inflammation, high androgen production, and PCOS in cycling women.
- **Quinolinate –** High quinolinate has been linked to inflammation, high androgen production, and PCOS in cycling women.
- **b-Hydroxyisovalerate –** Biotin deficiency can contribute to hair loss. If one of the patient's high androgen complaints includes hair loss, check for elevated b-hydroxyisovalerate.

In the example, the patient's Xanthurenate, Kynurenate, and Quinolinate are high. Abnormalities in tryptophan metabolism and high Quinolinate (possibly due to inflammation) may be contributing to her high androgen production.

See page 176 of the DUTCH Interpretive Guide to learn more about the Organic Acid Tests (OATs) and see pages 42-47 of the DUTCH Treatment Guide for treatment considerations relating to the OATs.

CORTISOL

9 Assess if cortisone (inactive) adds more insight to the free cortisol assessment

Does free cortisone add more insight to the free cortisol assessment? **Free cortisone (inactive)** in the urine and saliva reflects the free cortisol (active) that entered the kidneys or the saliva glands and was converted to cortisone locally before excretion. This makes free cortisone a secondary marker for free cortisol in circulation. In the example, the patient's Daily Free Cortisone Pattern (and 24hr Free Cortisone) are higher than the Daily Free Cortisol Pattern (and 24hr Free Cortisol); therefore, free cortisol in circulation may be higher than the Daily Free Cortisol Pattern (and 24hr Free Cortisol) imply.

See page 164 of the DUTCH Interpretive Guide to learn more about the Cortisone Shadow. See pages 34, 36-37, 60-62, 63 of the DUTCH Treatment Guide for general HPA axis support considerations, an herbal support overview, sleep and circadian rhythm support considerations, and stress and parasympathetic activity support considerations, respectively.

10 Assess if there is a whole-body preference for (inactive) cortisone or (active) cortisol

Is there a systemic preference for (inactive) cortisone or (active) cortisol? **The Systemic Preference** slider on the DUTCH Test is the best way to assess systemic preference. A Cortisol (THF) preference may occur when the body wants more cortisol in the active form (acute stressors) whereas a Cortisone (THE) preference may occur when the body wants less cortisol in the active form (chronic stressors). In the example, Cortisol (THF) and Cortisone (THE) are well-balanced as the Systemic Preference dial is at the 55th percentile.

See page 170 of the DUTCH Interpretive Guide to learn more about THE vs THF systemic preference. See pages 38 of the DUTCH Treatment Guide for treatment considerations relating to systemic preference.

11 Assess for anabolic-catabolic balance

Is there an **anabolic** or **catabolic** picture present? Compare the Total DHEA Production with the Total Cortisol Production (Metabolized Cortisol).

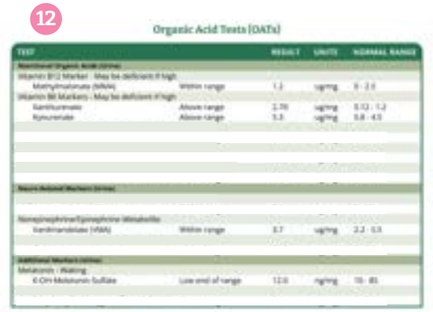
Cortisol > DHEA = Catabolic State
DHEA > Cortisol = Anabolic State

If there is relatively more cortisol than DHEA, the patient may be in a catabolic state. On the other hand, if there is relatively more DHEA than cortisol, the patient may be in an anabolic state. Excessive catabolism can result in the breakdown of body tissues, weakness, impaired tissue repair, and altered immune function. An anabolic state can promote gains in muscle mass from exercise and promote tissue repair. In the example, although the patient's Metabolized Cortisol is above range, their Total DHEA Production is also above range; thus, there is neither a strong anabolic nor catabolic picture present.

12 Assess whether any of the cortisol-related organic acids are out of range

Are any of the cortisol-related organic acids (MMA, Xanthurenate, Kynurenate, Melatonin, VMA) out of range?

- **Methylmalonate (MMA) –** High MMA may indicate B12 deficiency. High cortisol has been associated with reduced B12 in some studies.
- **Xanthurenate and Kynurenate –** High cortisol can impair tryptophan metabolism, causing Kynurenate and Xanthurenate to increase, without requiring B6 deficiency.
- **Vanilmandelate (VMA) –** During stress, epinephrine is released roughly 10 minutes before cortisol; Therefore, high VMA may be associated with high cortisol.
- **Melatonin –** Cortisol that is elevated at the end of the day can suppress melatonin production. High waking cortisol is often associated with higher overnight levels of cortisol which may also be suppressive to melatonin. Low melatonin accompanied with low morning cortisol has also been linked to poor sleep.



Page 6 of the report:
Organic Acid Tests (OATs)

In the example, the patient's Xanthurenate and Kynurenate are both high and Melatonin is low. High bedtime cortisol may be suppressing melatonin production.

See page 176 of the DUTCH Interpretive Guide to learn more about the Organic Acid Tests (OATs) and see pages 42-47 of the DUTCH Treatment Guide for treatment considerations relating to the OATs.

DUTCH STEROID PATHWAY

The DUTCH Steroid Pathway is a summary depicting where hormones come from and how they form through various cells in the body. It includes supplements, nutrients, herbs, and medications shown in the literature to increase or decrease particular enzymes affecting these hormones. This is a general steroid pathway and does not specifically differentiate from cells in the ovaries, adrenal glands, or testes.

HOW DO I READ THE CHART?

Begin at the top of the page with cholesterol and follow the arrows downstream to see the conversion of cholesterol into various steroid hormones. Hormones depicted with a **solid color bubble** are measured by the DUTCH Test, while hormones depicted with an **outline** are not. The outlined hormones are too far upstream to test directly with our methodology. Instead, we test the downstream metabolites of that hormone.

Hormones are color-coded for convenient reading:

- Cholesterol
- Pregnenolone
- Cortisol
- Progesterone
- Androgens
- Estrogen

Next to each arrow on the steroid pathway chart is the name of the protein responsible for moving each hormone further downstream. These proteins are important because they can be targeted with lifestyle changes and supplementation to improve symptoms associated hormone imbalances.

CONTRIBUTING FACTORS

1 3b-HSD

May be increased by: Fenugreek[1], high ACTH/hyperadrenalism[2], PCOS[3].
May be decreased by: Isoflavonoids/phytoestrogens[4], phthalates, organochlorines, BPA[5], ketoconazole[5], finasteride, dutasteride.

2 11b-HSD

May push to cortisone: EGCG[20], PCOS[8], curcumin[21], 7-keto-DHEA[19], progesterone[19], coffee[22], holy basil[23], bitter melon[24], hyperthyroidism[19, 26], high estrogens[19], glucocorticoids[19].
May push to cortisol: Insulin resistance, obesity[6, 17], inflammation[18], hypothyroidism[25], licorice root[19], phthalates, organotins, alkylphenols[19], mother's diet during pregnancy[19].

3 17b-HSD

May be increased by: Rutin[39], alcohol[41], abdominal obesity[42], bioflavonoids[43].
May be decreased by: Licorice[4, 34, 35], apigenin[4,38], phytoestrogens[43], atrazine[45].

4 17-hydroxylase

May be increased by: Hyperglycemia[27], hyperinsulinemia[28].

May be decreased by: Ketoconazole[29], spironolactone[30], apigenin, polyphenols[31, 32].

5 17, 20 Lyase

May be increased by: PCB exposure[33], DHEA supplements[7], obesity[34].

May be decreased by: Licorice root[34, 35], spironolactone[37], azole antifungals[38], hyperglycemia[27], apigenin[31, 38].

6 DHEA > DHEA-S (Hydroxysteroid Sulfotransferases + Steroid Sulfatase)

May be increased by: Spironolactone[84], dexamethasone[85], bile acid[86], St. John's Wort[84], forskolin[87].

May be decreased by: Low cysteine[88], inflammation[88], LPS[89], ketoconazole[88], progestin[88], licorice[90].

7 5a-Reductase & 5b-Reductase

5a-Reductase is best known because it makes androgens like testosterone more potent. It is also responsible for metabolizing progesterone and cortisol. If up-regulated, it may cause high androgen symptoms in men (thinning hair, prostate) and women (as in PCOS, thinning hair, acne, facial hair growth). 5b-Metabolites are less androgenic (weaker).

This same enzyme also metabolizes cortisol, see 8 for more detail.

5a may be increased by: Insulin resistance and obesity[6], DHEA supplementation[7], PCOS[8].

5a may be decreased by: Saw palmetto and beta-sitosterol[9], reishi[10], nettle root[11], Pygeum africanum[12], PUFA and EGCG[13].

5b may be increased by: Insulin resistance, high triglycerides[14], PCOS[15].

5b may be decreased by: Licorice[16].

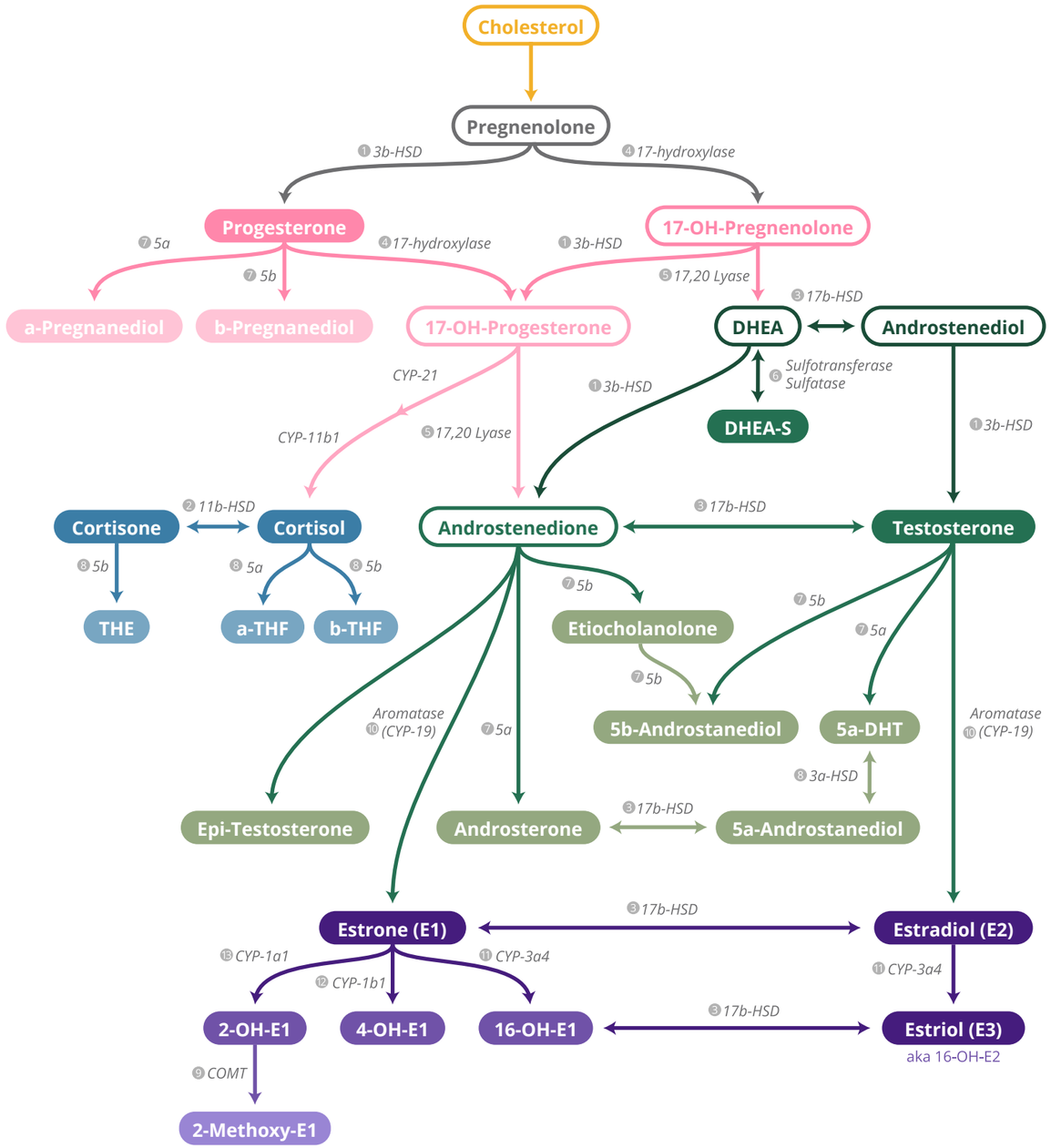
NOTE

> *5b-Reductase may be affected by some of the listed things for 5a as well (often to a lesser degree).*

8 Cortisol Metabolism/Clearance

Cortisol is metabolized by 5a/5b-reductase (and 3a-HSD) to a/b-THF & THE for excretion. Metabolism may be increased in obesity, high insulin and hyperthyroid. It may be slowed in cases of hypothyroidism, anorexia, cholestasis, or poor liver function.

This same enzyme metabolizes testosterone, androstenedione, and progesterone, see 7 for more detail.



9 COMT

May be increased by: SAM-e, magnesium, choline, B6, B12, folate, betaine/TMG (cofactors).

May be decreased by: Estradiol[80], phthalate esters[81], Rhodiola rosea, quercetin, catechin and epicatechin[83].

10 Aromatase (CYP-19)

May be increased by: Obesity and inflammation[46], high insulin[47], forskolin[48], quercetin, genistein (bioflavonoids)[49], white peony and licorice root[50], atrazine[51], rutin[39].

May be decreased by: Enterolactone, apigenin, genistein, chrysin and other flavonoids[52], white button mushrooms[53], grape seed extract, red wine procyanidin dimers[55], PCOS[56], antifungal medications[57], metformin[58], glyphosate[59], aromatase inhibitors (letrozole, anastrozole).

11 CYP-3a4

Many common medications **induce** CYP3A4, including but not limited to, phenobarbitol, phenytoin, rifampicin, and glucocorticoids.

Many common medications **interfere** with or competitively inhibit CYP3A4, including but not limited to, cimetidine, tamoxifen, quinolones, and fluoxetine.

May be increased by: St. John's wort[74], pesticides[75], caffeine[62], smoking[62], PAHs[74], moderate alcohol consumption[68], obesity[68].

May be decreased by: Grapefruit[60], resveratrol[60], rosemary[65], wild yam[77], peppermint oil[78], azole antifungals[79].

12 CYP-1b1

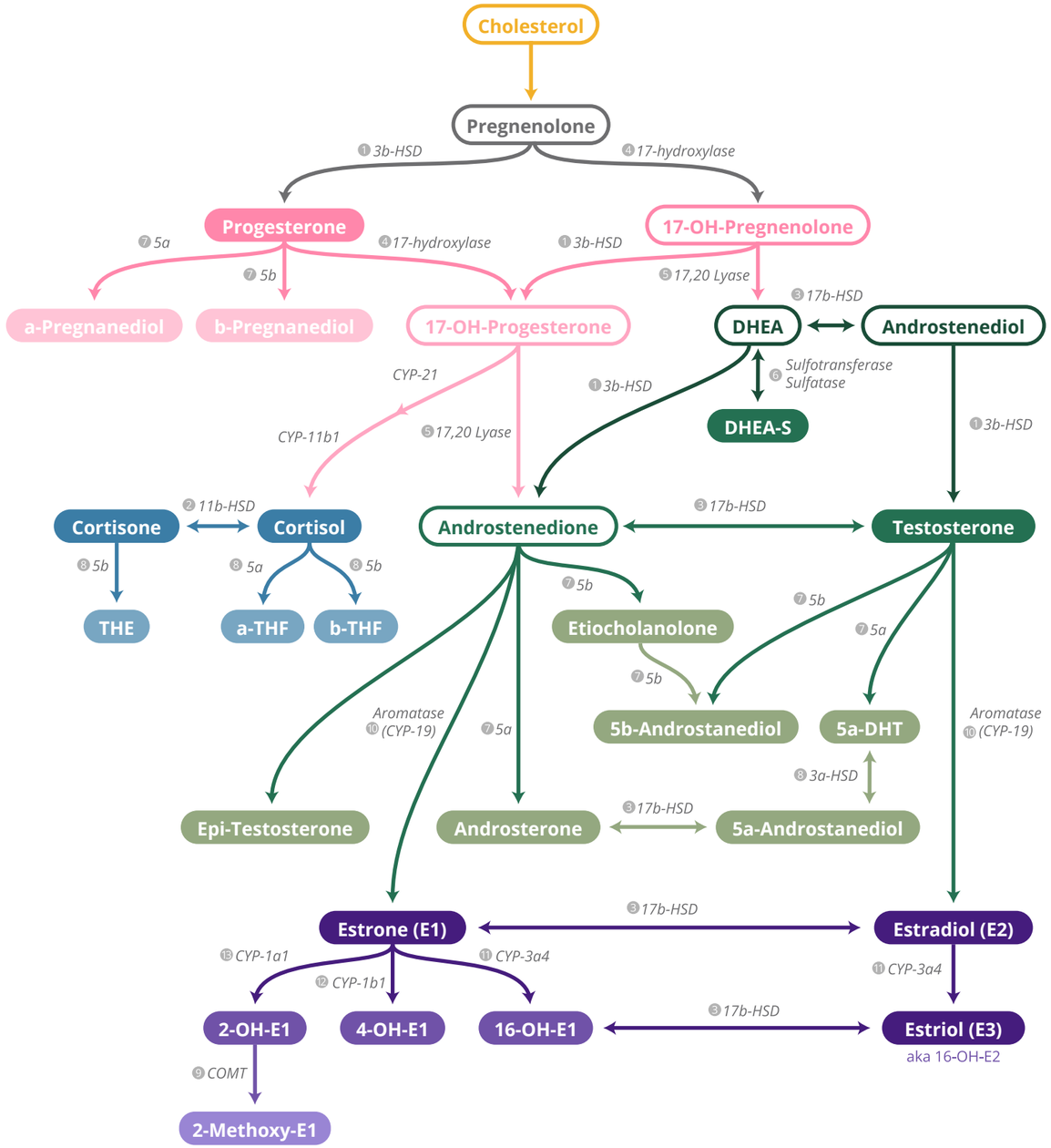
May be increased by: Inflammation[70], smoking[71], PAHs[69].

May be decreased by: Flavonoids[73], resveratrol[71].

13 CYP-1a1

May be increased by: Cruciferous vegetables[60], DIM/I3C[61], caffeine[62], soy[63], fish oil[64], rosemary extract[65], thyroxine[66], flaxseed[67].

May be decreased by: High sugar diet[67], moderate alcohol consumption[68], resveratrol and pterostilbene[69].



DUTCH HORMONE CONTINUUMS

The DUTCH Hormone Continuums consist of seven detailed, quick-reference handouts outlining the most common clinical drivers and associated signs and symptoms across low, optimal, and high levels of E2, progesterone, DHEA, testosterone, and cortisol.

CAUSES | CONTRIBUTORS TO PRE-MENOPAUSAL E2 STATUS

Very Low Below PMP

0.0-0.2 ng/mg

Ovaries NOT Cycling and Subphysiologic E2 Levels Due To:

- Low aromatase activity, such as with low body fat percentage [94]
- Very low DHEA [95]
- HPA axis suppressive medications, including glucocorticoids [99]
- Adrenal insufficiency, including Addison's Disease

Postmenopausal (PMP)

0.2-0.7 ng/mg

Ovaries NOT Cycling Due To:

- Conditions & medications that suppress the HPO axis, including combo OCPs [91]
- Diminished ovarian reserve, POI, perimenopause
- Low androgens affecting follicle development
- Medically induced, such as in oophorectomy [93]
- Hypogonadism, Hypopituitarism

Low

0.7-1.8 ng/mg

Ovaries Cycling but E2 is Low Due To:

- Incorrect timing of sample collection in the follicular phase (E2 reference range 1-2 ng/mg) [96]
- Conditions that impair (but do not fully suppress) the HPO axis [92]
- Low androgens affecting follicle development

Ovaries NOT Cycling but E2 Levels are Above the PMP Range Due To:

- High aromatase activity, typically obesity-related [102]

Normal

1.8-4.5 ng/mg

Ovaries Cycling and Producing Normal Luteal E2

Ovaries NOT Cycling but E2 levels are in the luteal range due to:

- Profound aromatase activity, typically obesity-related [102]
- Hormone therapy [104]

High

>4.5 ng/mg

Ovaries Cycling but E2 is High Due To:

- Incorrect timing of sample collection in the ovulatory phase (E2 reference range 4-12 ng/mg) [106]
- Perimenopause
- Metabolic issues, including obesity [103]
- High aromatase activity, typically obesity-related [102]
- Suboptimal estrogen detoxification
- Hormone therapy [104]

Ovaries NOT Cycling but E2 levels are above the luteal range due to:

- Hormone therapy [104]

Very High

Supraphysiologic E2 Levels Due To:

- Oral or sublingual estrogen therapy (1st pass affects urine metabolites only, not serum) [105]
- Pregnancy
- Hormone-producing neoplasms (rare)

EFFECTS | PRE-MENOPAUSAL E2-RELATED SIGNS & SYMPTOMS

Postmenopausal (PMP)

0.2-0.7 ng/mg

Low Estrogen Signs & Symptoms:

- Hot flashes and night sweats
- Vaginal dryness
- Mood disturbances (e.g., low mood or depression)
- Brain fog
- Low libido
- Insomnia
- Weight gain
- Joint pain
- Skin changes
- Decreased bone mineral density
- Increased cardiovascular risk

Low

0.7-1.8 ng/mg

Mildly Low Estrogen Signs & Symptoms:

- May or may not experience symptoms of low estrogen. Symptoms may be subtle or absent.
- Vaginal dryness
- Mood changes, including low mood
- Reduced libido

Normal

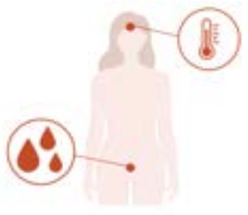
1.8-4.5 ng/mg

Normal Estrogen Levels are Associated With:

- Stable, positive mood
- Healthy energy levels
- Restorative sleep
- Normal sexual drive and function
- Weight management with a healthy lifestyle
- Healthy reproductive function
- Healthy cognition and memory
- Maintenance of bone mineral density, joint health, hair growth, skin elasticity, and more!

High

>4.5 ng/mg



High Estrogen Signs & Symptoms*:

- Heavy bleeding or prolonged menstrual bleeding
- Breast tenderness or fibrocystic changes
- Uterine fibroid growth
- Gallstones
- Increased risk of endometrial hyperplasia or cancer, and breast tumors or cancer

*An appropriate dose of oral or sublingual estradiol taken near the time of testing may increase urinary estrogen metabolites due to first-pass metabolism, without reflecting serum estradiol levels or causing symptoms of estrogen excess.

CAUSES | CONTRIBUTORS TO POST-MENOPAUSAL (PMP) E2 STATUS

Very Low Below PMP

0.0-0.2 ng/mg

Subphysiologic E2 Levels Due To:

- Low aromatase activity, such as with aromatase inhibiting pharmaceuticals [94]
- Very low adrenal DHEA [95]
- HPA axis suppressive medications, including glucocorticoids [99]
- Adrenal insufficiency, including Addison's Disease

Postmenopausal (PMP)

0.2-0.7 ng/mg

Normal PMP E2 Levels:

- Most PMP E2 originates from adrenal DHEA
- Patient may be on low-dose (localized) vaginal E2 therapy that does not increase systemic E2 levels

Mildly Above PMP

0.7-1.8 ng/mg

E2 Levels that are just above the PMP Range May be Normal for Some PMP Women [107]

E2 levels are mildly above the PMP range due to:

- High aromatase activity, typically obesity-related [102]
- Low-moderate dose E2 therapy [104]

Above PMP

1.8-4.5 ng/mg

E2 Levels are Significantly Above the PMP Range Due To:

- Moderate-high dose E2 therapy [104]
- Profound aromatase activity, typically obesity-related [102]
- Perimenopause: If <1.5 years from final menstrual period (FMP), consider endogenous production

High

>4.5 ng/mg

E2 Levels are Above the Luteal Range (very high for PMP) Due To:

- High dose E2 therapy [104]
- Perimenopause: If <1.5 years from FMP, consider endogenous production

Very High

Supraphysiologic E2 Levels Due To:

- Oral or sublingual estrogen therapy (1st pass affects urine metabolites only, not serum) [105]
- Hormone-producing neoplasms (rare)

EFFECTS | POST-MENOPAUSAL (PMP) E2-RELATED SIGNS & SYMPTOMS

Postmenopausal (PMP)

0.2-0.7 ng/mg

Low Estrogen Symptoms:

- Hot flashes, night sweats
- Vaginal dryness, vaginal atrophy
- Mood disturbances (depression)
- Brain fog
- Low sex drive
- Insomnia
- Weight gain
- Joint pain
- Skin issues
- Decreased bone mineral density
- Increased cardiovascular risk

High

>4.5 ng/mg

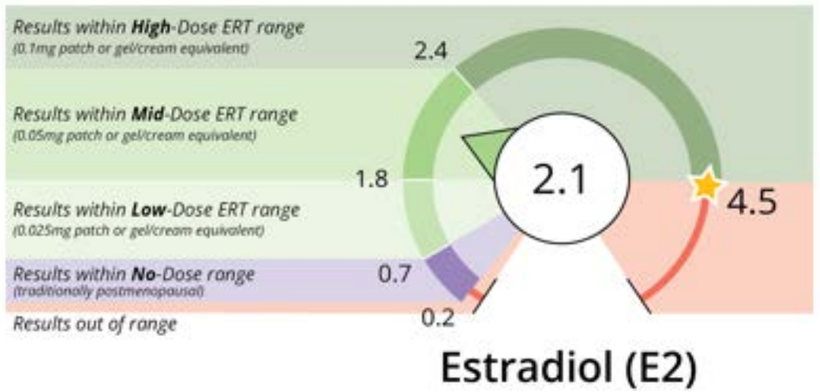
High Estrogen Symptoms*:

- Breakthrough bleeding, especially if not adequately opposed with progesterone
- Tender or fibrocystic breasts
- Uterine fibroid growth
- Gallstones
- Increased risk of endometrial hyperplasia or cancer, and breast tumors or cancer

*An appropriate dose of oral or sublingual estradiol taken near the time of testing may increase urinary estrogen metabolites due to first-pass metabolism, without reflecting serum estradiol levels or causing symptoms of estrogen excess.

PMP Levels with Estrogen Replacement Therapy (ERT)

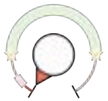
Observed Ranges



Healthy Estrogen Levels are Associated with:

- Positive mood
- Healthy energy levels
- Good sleep
- Modest sex drive and function
- Weight management with healthy lifestyle
- Good cognition, memory, bone density, joint health, hair growth, skin elasticity,
- and more!

CAUSES | CONTRIBUTORS TO PRE-MENOPAUSAL P4 STATUS



Very Low Below PMP

0.0-0.3 ng/mg

Ovaries are NOT cycling and Subphysiologic P4 Levels:

- Low output of other adrenal hormones, such as cortisol and DHEA, can be associated with very low P4

Anovulation

0.3-2.0 ng/mg

Ovaries are NOT Cycling Due To:

- Conditions & medications that suppress the HPO axis, including combo OCPs [91]
- High androgens inhibiting ovulation such as with PCOS
- Diminished ovarian reserve, POI, perimenopause
- Medically induced, as with oophorectomy [93]
- Hypogonadism
- Hypopituitarism

Ovaries are cycling but:

- The patient incorrectly timed the sample collection outside of their luteal phase [97]

Sub-optimal

2.0-6.0 ng/mg

Ovaries are cycling and Ovulation Occurred but P4 Levels are Suboptimal Due To:

- The patient incorrectly timed the sample collection in their early or late luteal phase (not mid-luteal) [117]
- Inadequate ovarian P4 production or luteal phase defect (LPD)
- Conditions that impair (but do not fully suppress) the HPO axis [92]

Ovaries are NOT cycling but P4 levels are above the PMP range due to:

- Elevated adrenal P4 output, typically stress-related [108]

Ovaries are NOT Cycling but P4 Levels are Above the PMP Range Due To:

- Progesterone [20] and pregnenolone therapy: The degree of elevation in urinary P4 metabolites depends on the route of administration (ROA) and dose. With oral use of progesterone, the Progesterone Serum Equivalent is not a valid concept and progesterone metabolite levels in urine will not correlate with serum progesterone. However, the P4 5a-Metabolism may provide insight into its sedating effects. Note that pregnenolone does not increase serum progesterone, but it increases progesterone metabolites on the DUTCH Test. [19]

Optimal

6-20 ng/mg

Ovaries are Cycling, Ovulation Occurred and P4 Levels are Optimal:

- Normal ovarian production of P4 during the luteal phase
- P4 >12 ng/mL may be optimal for fertility
- Note that P4 therapy may be bringing P4 levels into the normal range, in the presence of low endogenous corpus luteum P4 production

Oral Progesterone [110]

High

>20 ng/mg

Ovaries are Cycling, Ovulation occurred, but P4 Levels are Elevated Due To:

- Normal robust ovarian P4 production
- Ovarian cysts
- PCOS (some women)
- P4 therapy is increasing P4 on top of endogenous corpus luteum P4 production [110]

Very High

Supraphysiologic P4 Levels Due To:

- Oral or sublingual P4 or pregnenolone (1st pass affects urine metabolites only, not serum) [109, 110]
- Pregnancy
- Progesterone producing neoplasms (rare)

EFFECTS | PRE-MENOPAUSAL P4-RELATED SIGNS & SYMPTOMS

Anovulation

0.3-2.0 ng/mg

When P4 is Low/Suboptimal Relative to E2:

- Abnormal uterine bleeding (AUB)
- Increased endometrial cancer risk
- Breast tenderness
- PMS

When P4 is Low/Suboptimal with Concurrent Low E2:

- Symptoms of low E2
- Insomnia
- Fatigue
- Irritability, Anxiety
- Low bone mineral density (BMD)

Sub-optimal

2.0-6.0 ng/mg

When P4 is Low/Suboptimal Relative to E2:

- Abnormal uterine bleeding (AUB)
- Increased endometrial cancer risk
- Breast tenderness
- PMS

When P4 is Low/Suboptimal with Concurrent Low E2:

- Symptoms of low E2
- Insomnia
- Fatigue
- Irritability, Anxiety
- Low bone mineral density (BMD)

Optimal

6-20 ng/mg

Healthy P4 Levels Balanced with E2 are Associated with the Following:

- Regular cycles (25-35 days)
- Cycles are predictable within 1-2 days
- Mild premenstrual symptoms 2-3 days before menses (breast tenderness, fluid retention, bloating) is more consistent with ovulation and healthy progesterone than an absence of symptoms
- Absence of spotting or AUB Levels <12ng/mg may be suboptimal for fertility

Oral Progesterone: [110]

- Laboratory P4 measurement cannot predict endometrial protection

High

>20

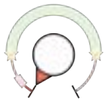
High P4 Due to Ovulation is Often Normal & Not Problematic

High progesterone signs & symptoms*:

- Fatigue
- Increased appetite
- Breast tenderness
- Bloating
- More significant symptoms of PMS

*An appropriate dose of oral or sublingual progesterone taken near the time of testing may increase urinary progesterone metabolites due to first-pass metabolism, without reflecting serum progesterone levels or causing symptoms of progesterone excess.

CAUSES | CONTRIBUTORS TO POST-MENOPAUSAL P4 STATUS



Very Low Below PMP

0.0-0.3 ng/mg

Subphysiologic P4 Levels:

- Low output of other adrenal hormones, such as cortisol and DHEA, can be associated with very low P4, but the difference in P4 is clinically inconsequential

Postmenopausal (PMP)

0.3-2.0 ng/mg

P4 levels are Normal for PMP status:

- Adrenal output supplies all postmenopausal progesterone

Mildly Above PMP

2.0-6.0 ng/mg

P4 Levels are Above the PMP Range but Below the Luteal Range Due To:

- High adrenal P4 output, typically stress-related [108]
- Transdermal progesterone can result in mild elevations in P4 levels in both urine and serum testing
- OMP skipped on day of testing or lower dose (<100 mg)

Above PMP

6-20 ng/mg

Oral Progesterone:

- When patients report taking oral micronized progesterone (OMP) within 72 hours of collection, adjusted OMP reference ranges are reported [110]

High

>20 ng/mg

Supraphysiologic P4 Levels Due To:

- Oral or sublingual progesterone or pregnenolone therapy (1st pass affects urine metabolites only, not serum) [109, 110]
- Progesterone producing neoplasms (rare)

P4 levels are Above the PMP Range Due To:

- Progesterone therapy [110] - and pregnenolone therapy - The degree of elevation in urinary P4 metabolites depends on the route of administration (ROA) and dose. With oral use of progesterone, the Progesterone Serum Equivalent is not a valid concept and will not correlate with serum progesterone. However, the P4 5a-Metabolism may provide insight into its sedating effects. Note that pregnenolone does not increase serum progesterone, but it increases progesterone metabolites on the DUTCH Test. [109]
- Perimenopause: If not >1.0-1.5 years out from final menstrual period (FMP), consider endogenous ovarian production

EFFECTS | POST-MENOPAUSAL (PMP) P4-RELATED SIGNS & SYMPTOMS

Postmenopausal (PMP)

0.3-2.0 ng/mg

PMP P4 Levels are Considered "Not Clinically Impactful":

- These P4 levels provide no protection against endometrial hyperplasia or cancer in women on estrogen (E2) therapy or with elevated E2 due to obesity.
- Due to progesterone's rapid pharmacokinetics, serum levels may appear low even with oral dosing, depending on the timing of the test relative to administration.

High

>20 ng/mg

Too Much P4 Supplementation May Result in High Progesterone Symptoms*:

- Fatigue, drowsiness, dizziness may be resolved by dosing at night (if dosing in the morning)
- Increased appetite
- Breast tenderness
- Bloating

*An appropriate dose of oral or sublingual P4 taken near the time of testing may increase urinary P4 metabolites due to first-pass metabolism, without reflecting serum P4 levels or causing symptoms of P4 excess.

Supplemented P4

Oral Progesterone:

- When patients report taking oral micronized progesterone (OMP) within 72 hours of collection, adjusted OMP reference ranges are reported [110]

Regarding endometrial protection in women with a uterus:

Laboratory P4 measurement cannot predict endometrial protection. Studies performing endometrial biopsies on patients to monitor oral and vaginal micronized progesterone therapy (OMP and VMP) with concomitant E2 therapy have found the following P4 dosing and ROAs to be uterine protective:

- 100 mg OMP nightly or 200 mg OMP 12 consecutive nights per month
- 200 mg OMP nightly may be more uterine-protective with higher dose E2 therapy
- 100 mg VMP 12 consecutive nights per month
- 200 mg VMP 12 consecutive nights per month may be more uterine-protective with higher dose E2 therapy

Adequate P4 Supplementation (See OMP and VMP Dosing Above):

- Protects the endometrium from hyperplasia and cancer with E2 therapy
- May reduce hot flashes, anxiety and irritability, support sleep and bone mineral density

CAUSES | CONTRIBUTORS TO DHEA STATUS IN WOMEN

Very Low

Subphysiologic DHEA Levels Due To:

- Pituitary or hypothalamic suppression
- Medications that suppress the HPA axis (e.g., higher-dose or prolonged glucocorticoids, opioids, etc.) [99]
- Adrenal insufficiency, including Addison's disease
- Adrenalectomy

Low

<500 ng/mg

Low DHEA Levels Due To:

- Accelerated age-related decline in DHEA production from the zona reticularis
- Significant chronic HPA axis dysfunction (e.g., prolonged stress, sleep deprivation, chronic inflammation, etc.) [98]
- Medications that impair (but do not fully suppress) the HPA axis (e.g., lower-dose glucocorticoids, opioids, etc.) [99]
- Conditions that slow the cortisol clearance rate (CCR), including hypothyroidism [100]
- Pituitary or hypothalamic dysfunction

Postmenopausal (PMP)

500-1680 ng/mg

PMP DHEA Levels:

- Common and expected with aging, particularly in women over age 40
- Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range

Lower than Expected DHEA (e.g., women under age 40 or not PMP) Due To:

- Mild chronic HPA axis dysfunction [98]
- Medications that mildly impair (but do not fully suppress) the HPA axis (e.g., lower-dose glucocorticoids, opioids, etc.) [99]
- Accelerated age-related decline in DHEA production from the zona reticularis
- Conditions that slow the cortisol clearance rate (CCR), including hypothyroidism [100]

Optimal Pre-Menopausal

1260-3000 ng/mg

Premenopausal DHEA Levels:

- Expected in women age 40 and younger
- Associated with normal adrenal androgen production
- Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range

High

>3000 ng/mg

High DHEA Levels Due To:

- Significant acute HPA axis activation or dysfunction [111]
- Hyperprolactinemia
- Adrenal-driven PCOS
- Conditions that increase the cortisol clearance rate (CCR) such as obesity or metabolic disease [112]
- CAH/NCCAH [113]
- Cushing's Syndrome (not due to exogenous glucocorticoid use) [115]

Very High

Supraphysiologic DHEA Levels Due To:

- Oral or sublingual DHEA or T therapy (1st pass increases urine metabolites only, not serum) [114]
- DHEA secreting neoplasms (rare)

EFFECTS | DHEA-RELATED SIGNS & SYMPTOMS IN WOMEN

Low

<500 ng/mg

Low DHEA Signs & Symptoms:

- Impaired fertility in premenopausal women
- Hypoactive sexual desire disorder (HSDD) or low libido
- Increased risk of metabolic or cardiovascular disease
- Fatigue and brain fog
- Cognitive decline or memory difficulties
- Reduced psychological well-being
- Mood issues, including low mood or anxiety
- Immune dysregulation

Postmenopausal (PMP)

500-1680 ng/mg

Low(er) DHEA:

- Some women – particularly younger, cycling women under age 40 - may be more likely to experience symptoms of low DHEA.

Optimal Pre-Menopausal

1260-3000 ng/mg

Healthy DHEA Levels Support:

- Healthy estrogen levels
- Maintenance of the majority of female testosterone
- Maintenance of muscle mass, if exercising
- Preservation of bone mineral density
- Maintenance of insulin sensitivity
- Psychological well-being and mood stability

High

>3000 ng/mg

High DHEA Signs & Symptoms:*

- Mild androgen excess may present as acne, hirsutism, scalp hair thinning
- Menstrual irregularities
- Impaired fertility (in premenopausal women)
- In severe cases, virilization (e.g., voice deepening, clitoral enlargement)
- May contribute to elevated estradiol (E2) and testosterone (T) levels

*An appropriate dose of oral or sublingual DHEA or T taken near the time of testing may increase urinary DHEA metabolites due to first-pass metabolism, without reflecting serum DHEA levels or causing symptoms of androgen excess.

CAUSES | CONTRIBUTORS TO TESTOSTERONE STATUS IN WOMEN

Very Low

Very Low T Levels (in urine):

- Confirm with serum testing. A genetic deletion polymorphism in the UGT2B17 gene can lead to very low urinary excretion of testosterone even when serum levels are normal
- If accurate, refer to the possible contributors seen under "Low".

Optimal Pre-Menopausal

4.0-14 ng/mg

Premenopausal T Levels:

- Expected in women age 40 and younger
- Associated with normal adrenal and ovarian androgen production
- Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range

Low

<2.3 ng/mg

Low T Levels Due To:

- Conditions & medications that suppress the HPO axis, including combo OCPs [91]
- Diminished ovarian reserve, POI, perimenopause
- Low adrenal androgens that are precursors to T (e.g., DHEA, A4)
- Accelerated age-related decline in T production from the adrenals and ovaries
- Medically induced, such as in oophorectomy [93]
- High SHBG (as seen with combo OCPs or oral estrogens) [101]
- Hypogonadism
- Hypopituitarism
- Medications that suppress the HPA axis (e.g., higher-dose or prolonged glucocorticoids, opioids, etc.) [99]

High

>14 ng/mg

High T Levels Due To:

- Metabolic issues as seen with PCOS and obesity
- Low SHBG (as seen with PCOS and insulin resistance) [116]
- High adrenal androgens that are precursors to T (e.g., DHEA, A4)
- Suboptimal T detoxification adding to the high T levels
- Pregnancy
- Low aromatase activity (less T → E) [94]
- Hormone therapy is increasing T on top of high endogenous T production
- CAH/NCCAH [113]

Postmenopausal (PMP)

2.3-6.3 ng/mg

PMP T Levels:

- Common and expected with aging, particularly in women over age 40
- Women aged 41-55 may fall within or below the optimal pre-menopausal androgen range

Lower than Expected T (e.g., women under age 40) Due To:

- Conditions that impair (but do not fully suppress) the HPO axis [92]
- High SHBG (as seen with combo OCPs or oral estrogens) [101]
- Low adrenal androgens that are precursors to T (e.g., DHEA, A4)
- Mild chronic HPA axis dysfunction [98]
- Medically induced, such as in oophorectomy [93]
- Accelerated age-related decline in T production from the adrenals and ovaries
- High aromatase activity (more T → E) , typically obesity-related [102]
- Medications that mildly impair (but do not fully suppress) the HPA axis (e.g., lower-dose glucocorticoids, opioids, etc.) [99]

Very High

Supraphysiologic T Levels Due To:

- Oral or sublingual DHEA or T therapy (1st pass increases urine metabolites only, not serum) [114]
- CAH/NCCAH [113]
- Androgen-secreting neoplasms (rare)

EFFECTS | TESTOSTERONE-RELATED SIGNS & SYMPTOMS IN WOMEN

Low

<2.3 ng/mg

Low T Signs & Symptoms:

- Impaired fertility in premenopausal women
- Increased pregnancy loss
- Reduced psychological well-being
- Mood issues, including low mood
- Fatigue
- Reduced bone mineral density and muscle mass
- Hypoactive sexual desire disorder (HSDD) or low libido

Optimal Pre-Menopausal

4.0-14 ng/mg

Healthy T Levels Support:

- Normal sexual function
- Maintenance of muscle mass, if exercising
- Preservation bone mineral density
- Maintenance of insulin sensitivity
- Psychological well-being and mood stability

Postmenopausal (PMP)

2.3-6.3 ng/mg

Low(er) T:

- Some women – particularly younger, cycling women under age 40 - may be more likely to experience symptoms of low T
- Reduced psychological well-being
- Mood issues, including low mood
- Fatigue
- Reduced bone mineral density and muscle mass
- Hypoactive sexual desire disorder (HSDD) or low libido

High

>14 ng/mg

High T Signs & Symptoms:*

- Hirsutism (body and facial hair growth)
- Androgenic alopecia (scalp hair loss)
- Acne
- Menstrual irregularities or no cycles (amenorrhea)
- Impaired fertility in premenopausal women
- In severe cases, virilization (e.g., voice deepening, clitoral enlargement)
- May contribute to elevated estradiol (E2) levels

*An appropriate dose of oral or sublingual T or DHEA therapy taken near the time of testing may increase urinary T metabolites due to first-pass metabolism, without reflecting serum T levels or causing symptoms of androgen excess.

CAUSES | CONTRIBUTORS TO CORTISOL STATUS IN MEN & WOMEN

Very Low

Very Low Cortisol Due To:

All of the "Low" contributors, typically more severe or prolonged, and/or:

- Pituitary or hypothalamic suppression
- Medications that suppress the HPA axis (e.g., higher-dose or prolonged glucocorticoids, opioids) [99]
- Adrenal insufficiency, including Addison's disease

Low

Low Cortisol Due To:

- Burnout and prolonged stress
- Chronic sleep deprivation or untreated sleep apnea
- Chronic infection, pain, or inflammation
- Pituitary or hypothalamic dysfunction
- Medications that impair (but do not fully suppress) the HPA axis (e.g., glucocorticoids, opioids) [99]
- Traumatic brain injury, concussions, PTSD
- CAH / NCCAH [113]

Normal

Habits That Promote Healthy Cortisol Levels:

- Practicing effective stress management
- Maintaining a consistent sleep schedule with adequate, restorative sleep
- Eating regular, balanced meals to support stable blood sugar
- Getting morning light exposure and limiting late-night light
- Engaging in regular, moderate physical activity (avoiding chronic overtraining)
- Prioritizing recovery, rest days, and downtime
- Supporting immune health through nutrition and illness recovery
- Maintaining emotional regulation and psychological resilience
- Limiting excessive caffeine and alcohol intake
- Building predictable daily routines to support circadian rhythm

High

High Cortisol Due To:

- Acute psychological stress
- Blood sugar dysregulation
- Acute inflammation
- Acute pain
- Acute infection or illness
- Elevated blood pressure
- Caffeine and other stimulants
- Cushing's syndrome
- Oral or systemic hydrocortisone use
- Strenuous or excessive exercise

Very High

Very High Cortisol Due To:

- Extreme acute psychological stress
- Acute inflammation
- Acute pain
- Acute infection or illness
- Cushing's syndrome
- Oral or systemic hydrocortisone use

Oral hydrocortisone supplementation:

It is important that you know when the patient last took their hydrocortisone therapy to properly interpret the results. Urinary Free Cortisol and Free Cortisone will likely be elevated for 4-6 hours after supplementation and urinary Metabolized Cortisol will likely be elevated for 10-12 hours after supplementation. Samples collected more than 10-12 hours after supplementation should be considered baseline (non-supplementing) values. Be aware that cortisol metabolites will lag behind free cortisol levels, so elevations in cortisol metabolites may be due to supplementation that is no longer affecting free cortisol levels if taken the morning of the test.

EFFECTS | CORTISOL-RELATED SIGNS & SYMPTOMS IN MEN & WOMEN

Low

Low Cortisol Levels May Lead To:

- Persistent fatigue and burnout
- Low mood or depression
- Reduced motivation and drive
- Low libido
- Sleep issues
- Low blood pressure
- Dizziness or lightheadedness
- Weakness or fainting
- Poor exercise tolerance
- Impaired cardiovascular and immune function

High

High Cortisol Levels May Lead To:

- Anxiety, panic attacks, or depression
- Insomnia or non-restorative sleep
- Weight gain, particularly central (abdominal) fat
- Brain fog and memory difficulties
- Increased inflammation
- Blood sugar and insulin dysregulation
- High blood pressure
- Hair thinning or loss
- Digestive complaints
- Reduced bone mineral density

Normal

Healthy Levels of Cortisol Support:

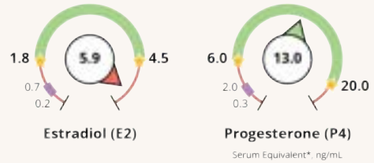
- Stable energy throughout the day
- Normal stress resilience and emotional regulation
- Restful, restorative sleep with a normal circadian rhythm
- Healthy blood sugar regulation
- Normal blood pressure and cardiovascular support
- Appropriate immune and inflammatory responses
- Clear thinking, focus, and memory
- Balanced mood and motivation
- Normal metabolism and weight regulation
- Healthy response to illness, injury, and physical exertion

DUTCH PATTERN INTERVENTION CHART

The DUTCH Pattern Intervention Chart serves as a convenient reference guide to help interpret and address key findings from DUTCH Test reports. Beneath each of the common DUTCH hormone patterns, find real report examples to help you quickly recognize them in patient results, followed by corresponding treatment ideas and intervention options tailored to each pattern. For more in-depth potential support considerations, see the DUTCH Treatment Guide.

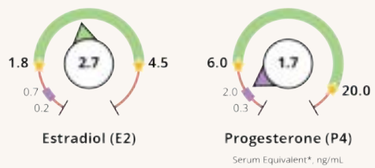
ESTROGEN & PROGESTERONE

ESTROGEN DOMINANCE PATTERNS



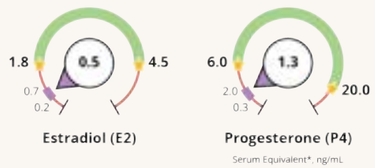
- **Phase 1 Support:** DIM/I3C, sulforaphane, citrus bioflavonoids
- **Phase 2 Support:** Methylated Bs, TMG, Mag
- **HPO Axis Supports:** Myoinositol, Vit D, Zinc
- **Decrease Aromatase:** Bioflavonoids, Damiana
- Progesterone therapy

LOW PROGESTERONE IN CYCLING WOMEN



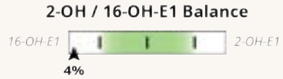
- **HPO Axis Supports:** Myoinositol, Vit D, Zinc
- **Ovulation Supports:** Maca, Shatavari, Tribulus,
- **Phytoprogestogens:** Blue cohosh, Chaste tree berry, Fenugreek, Sarsaparilla, Wild Yam, Yucca
- Progesterone therapy

LOW ESTROGEN & PROGESTERONE IN LATE PERI & MENOPAUSE



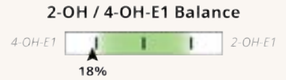
- Estradiol therapy
- Progesterone therapy
- **Phytoestrogens:** Alfalfa, Dong Quai, Fennel, Fenugreek, Flaxseeds, Fo-Ti, Gamma oryzanol, Licorice, Red Clover, Resveratrol, Sage
- **Phytoprogestogens:** Blue cohosh, Chaste tree berry, Fenugreek, Sarsaparilla, Wild Yam, Yucca

PHASE 1 LOW 2:16 RATIO



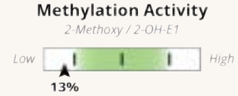
- **16-OH-E1 reducers:** DIM, Grapefruit, Resveratrol, Rosemary, Sulforaphane, Wild Yam
- **2-OH pathway supports:** Cruciferous vegetables, DIM/I3C, Caffeine, Soy, Fish oil, Rosemary extract, Thyroxine, Flaxseed
- Reduce inflammation, EDC exposures, mold toxins

PHASE 1 LOW 2:4 RATIO



- **4-OH-E1 reducers:** Bioflavonoids, Resveratrol
- **DNA protectors:** Glutathione, N-acetylcysteine (NAC), Sulforaphane
- **2-OH pathway supports:** Cruciferous vegetables, DIM/I3C, Caffeine, Soy, Fish oil, Rosemary extract, Thyroxine, Flaxseed
- Reduce inflammation, EDC exposures, mold toxins

PHASE 2 LOW COMT ACTIVITY



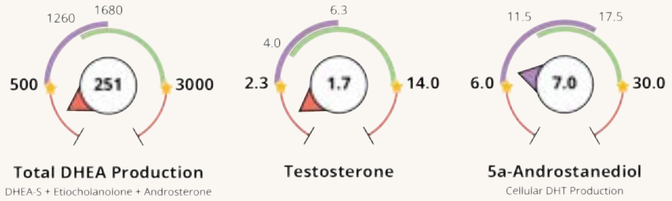
- Methylated B Complex
- B6, Methylfolate, B12 (methyl-, hydroxo-)
- Methionine, Taurine
- SAMe
- Trimethylglycine (TMG)

NOTE

Any factors that influence hormone ratios can also affect the absolute levels of those hormones. Therefore, ratios should always be evaluated in conjunction with whether the individual hormone and metabolite levels are low, normal, or high.

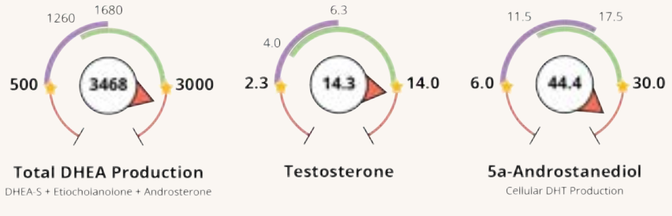
ANDROGENS

LOW ANDROGENS



- **Androgen-Supporters:** Ashwagandha, Damiana, Epimedium, Fenugreek , Indian coleus, Korean Ginseng, Maca, Mucuna, Sarsaparilla, Shatavari (Females), Tongkat Ali, Tribulus, Yohimbe
- DHEA Therapy
- Testosterone Therapy

HIGH ANDROGENS



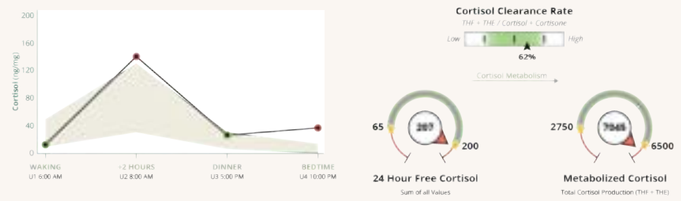
- **Increase SHBG:** DIM, Omega-3, Soy isoflavones
- **Support insulin sensitivity:** a-Lipoic Acid, Berberine, Myoinositol
- **Support aromatase:** Licorice, White Peony
- **Increase sulfation:** Methionine, Molybdenum, MSM, NAC, Sulforaphane, Taurine
- **Reduce stress/HPA:** Holy basil, Maca, Magnolia, Reishi, Rhodiola

REDUCING 5A-REDUCTASE ACTIVITY

- **Inhibit 5aR:** Green Tea Extract, Nettle Root, Pygeum africanum, Reishi, Saw Palmetto
- **Support insulin sensitivity:** Berberine, a-Lipoic Acid, Myoinositol
- **Reduce inflammation:** Curcumin, Ginger, Omega-3/SPM

CORTISOL

HIGH CORTISOL LEVELS



- **Cortisol-calming Supports:** Ashwagandha, Bacopa, Holy basil, Jujube, Lavender, Lemon balm, L-theanine, Magnolia bark, Phosphatidylserine, Skullcap, Valerian
- **Calming nutrition:** B complex, Choline, Fish Oil, Magnesium, Vit C, Zinc
- **Lifestyle:** Sleep supports, Stress-relieving practices (meditation, journaling, yoga)

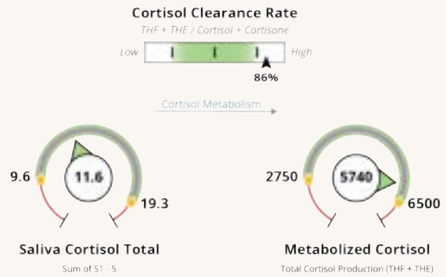
LOW CORTISOL LEVELS

- **Cortisol-stimulating Supports:** Cordyceps, Korean Ginseng, Licorice, Reishi, Rhodiola, Schisandra, Siberian ginseng
- **Nutritional Adrenal Supports:** Adrenal cortex glandulars, B5, B6, Fish Oil, Mitochondrial Supports, PABA, Vit C
- **Lifestyle:** Light therapy, Morning exercise

NOTE

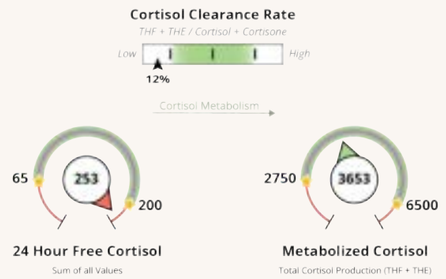
Very low cortisol levels (<10 ng/mg 24 Hour Free Cortisol; <1,000 ng/mg Metabolized Cortisol) may be due to HPA axis suppression.

HIGH CORTISOL CLEARANCE RATE



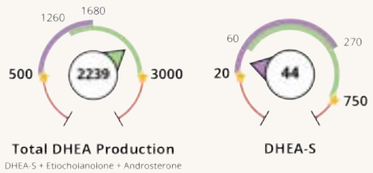
- **Inflammation contributing:** Curcumin, Green Tea Extract
- **High Insulin contributing:** Bitter melon, Cinnamon, Gymnema
- **High BMI contributing:** a-Lipoic Acid, Curcumin, GLP-1 Supportive Microbes, Melatonin, Zinc
- **Hyperthyroid contributing:** Medication management, Lemon balm, Lycopus, Magnesium, Motherwort, N-acetylcysteine (NAC), Selenium

LOW CORTISOL CLEARANCE RATE



- **Hypothyroid contributing:** Medication management, Iodine, Tyrosine, Thyroid glandulars, B Complex, Vit A, Vit C, Vit E, Selenium, Zinc
- **Iron deficiency contributing:** B6, Iron, Magnesium, Zinc
- **Sluggish liver activity:** Burdock, Butyrate, Curcumin, Dandelion root, Glutathione, Humic/Fulvic Acids, Methionine, Milk thistle, Taurine
- Ensure adequate daily caloric intake

LOW SULFATION



- Methionine
- Molybdenum
- MSM
- N-acetylcysteine (NAC)
- Taurine
- Reduce Inflammation
- Reduce EDC exposures

ORGANIC ACIDS

HIGH MMA/LOW B12

- Adenosylcobalamin, Hydroxycobalamin, Methylcobalamin

HIGH XANTHURENATE & HIGH KYNURENATE/LOW B6

- **Supplement with B6:** P5P, Pyridoxine
- Reduce inflammation

HIGH PYROGLUTAMATE/LOW GLUTATHIONE

- **Glutathione Supports:** B2, B6, Curcumin, Glycine, Green Tea, Glutathione, N-acetylcysteine (NAC), Selenium, Sulforaphane, Vit C, Vit E, Zinc

HIGH B-HYDROXYISOVALERATE/LOW BIOTIN

- Supplement with Biotin

HIGH INDICAN/DYSBIOSIS

- Consider stool testing
- **Gut Health Supports:** Fiber+hydration, Pre+probiotics, Resistant starches, Calcium-d-glucarate (if high b-glucuronidase), Milk thistle

NEUROTRANSMITTER IMBALANCE

Low HVA and/or VMA

- Support Cortisol if low and support COMT
- **Support dopamine, NE, and EPI production:** B complex, DLPA, Iron if low, Mucuna (contains L-DOPA), Tyrosine, Vitamin C

High HVA and/or VMA

- Stress reduction and support COMT
- **Support dopamine, NE, and EPI clearance:** B vits (B2, B3, B6), Lithium orotate, Magnesium

LOW MELATONIN

- Melatonin therapy
- **Support production:** 5-HTP, Tryptophan, Vit B6, Vit D

HIGH 8-OHDG/OXIDATIVE STRESS

- **Support with Antioxidants:** Alpha lipoid acid (ALA), B complex, Colorful fruits and vegetables, Curcumin, Glutathione, Green tea, Magnesium, NAC, Resveratrol, Selenium, Sulforaphane, Taurine, Vit C, Vit E, Zinc

NOTES

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91. **Suppression of the hypothalamic-pituitary-ovarian (HPO) axis:** Due to medications (e.g., combination contraceptives like OCPs, vaginal rings, or patches containing progestin + ethinyl estradiol; progestin-only injections; GnRH agonists), severe stress/anxiety, significant weight loss, very low body weight or calorie intake, strenuous exercise, full-time breastfeeding, significant hyperprolactinemia, severe hypothyroidism, trauma, infections, or tumors.
92. **Impairment (but not complete suppression) of the hypothalamic-pituitary-ovarian (HPO) axis:** Medications (e.g., progestin IUDs, mini-pills), stressors (anxiety, strenuous exercise, weight loss, low body weight or calorie intake, trauma, tumors, infections), breastfeeding, hyperprolactinemia, hypothyroidism, or perimenopause.
93. **Medically induced:** Oophorectomy, radiation, or chemotherapy.
94. **Low aromatase activity:** Genetic/epigenetic factors, aromatase-inhibiting medications, or very low body fat percentage. Aromatase converts androgens like testosterone and DHEA (via androstenedione) into estrogens like estradiol and estrone.
95. **Very low androgens (especially adrenal DHEA):** Resulting from chronic HPA axis dysfunction (e.g., chronic stressors, burnout, systemic illness) or exogenous HPA axis-suppressive medications (e.g., glucocorticoids, opioids).
96. **Timing of collection:** During early follicular phase (reference range for E2 1–2 ng/mg).
97. **Timing of collection:** Follicular or ovulatory phases before corpus luteum production of progesterone has begun (reference range for b-pregnanediol 100–300 ng/mg; and a-pregnanediol 25–100 ng/mg).
98. **Chronic HPA axis dysfunction:** Due to ongoing stressors, burnout, or systemic illness, leading to reduced adrenal DHEA production.
99. **HPA axis exogenous suppression:** Synthetic glucocorticoids or opioids (degree of suppression depends on dose, frequency, and timing).
100. **Factors contributing to low (slower clearance) Cortisol Clearance Rate (CCR):** Hypothyroidism, liver and gallbladder stasis, anorexia.
101. **High SHBG contributors:** HIV, liver disease, hyperthyroidism, high estrogen/oral estrogens (e.g., combo OCPs and oral estrogen therapy), anticonvulsants, low testosterone, aging, smoking.
102. **Increased aromatase activity:** Genetic/epigenetic factors, high body fat and obesity, insulin resistance, or inflammation. In obese non-cycling women with high androgens, E2 more often falls in the 0.7–1.8 ng/mg range rather than higher.
103. **Metabolic conditions:** Insulin resistance, diabetes, obesity, inflammation, and PCOS.
104. **Hormone therapy:** Estrogen (E2) therapy; High dose and/or long-term testosterone and DHEA therapy can influence estrogen levels through aromatization. E2 therapy that is not adequately balanced with progesterone may increase risk for endometrial hyperplasia and cancer in women with a uterus. Research shows that 100 mg of oral progesterone nightly, 200 mg of oral progesterone nightly or 12 consecutive days per month, or 100-200 mg vaginal progesterone 12-14 consecutive days per month protects the endometrium. Higher FDA-approved E2 doses (e.g., 0.1 E2 TD patch) may require higher OMP dosing nightly (e.g., 200 mg OMP) for adequate endometrial protection.

105. **Oral/sublingual E2 therapy within 3 days of testing:** Causes significant elevation of estrogen metabolites due to first-pass metabolism in gut and liver. DUTCH E2 no longer correlates with serum levels, but metabolism patterns (phase 1 and 2) remain evaluable; metabolites clear in ~3 days.
106. **Timing of collection:** During ovulatory phase (reference range for E2 is 4–12 ng/mg).
107. **Clinical note:** E2 just above postmenopausal range may be normal in some postmenopausal women, however, E2 above the PMP range that is not adequately balanced with progesterone may increase risk for endometrial hyperplasia and cancer in women with a uterus.
108. **High adrenal progesterone output:** Common in anovulatory women due to stress or elevated cortisol.
109. **Pregnenolone supplementation:** Significantly raises urinary progesterone metabolites without substantially increasing serum progesterone.
110. **Oral/sublingual progesterone therapy within 3 days of testing:** Markedly elevates metabolites due to first-pass metabolism; DUTCH P4 levels no longer correlate with serum, but P4 metabolism patterns remain evaluable (evaluated via the "5a-Metabolism (P4)" slider bar on page #2 of a DUTCH Complete or DUTCH Plus). Clearance of P4 metabolites from the body takes ~3 days. When patients report oral micronized progesterone (OMP) within 72 hours of collection: Adjusted OMP reference ranges apply (b-pregnanediol 2,000–9,000 ng/mg; a-pregnanediol 580–3,000 ng/mg for standard 100 mg dose). Note that DUTCH P4 results CANNOT provide insight into the effects of supplemented progesterone (P4) on endometrial protection.
111. **Acute HPA axis activation:** Stress, anxiety, illness, or pain increasing adrenal DHEA output.
112. **Factors contributing to high (faster clearance) Cortisol Clearance Rate (CCR):** Obesity, hyperthyroidism (or excess thyroid medication), fatty liver, insulin resistance, inflammation.
113. **Congenital adrenal hyperplasia (CAH/NCCAH):** 21-Hydroxylase deficiency (21OHD) is the most common cause of Congenital Adrenal Hyperplasia (CAH) (severe), and Non-Classical Congenital Adrenal Hyperplasia (NCCAH) (milder). With 21OHD, the Total DHEA Production and testosterone are usually elevated due to ACTH-driven overproduction of adrenal androgens (DHEA and Androstenedione (A4)) as precursors are shunted away from cortisol synthesis. Note that DHEA-S levels may vary.
114. **Oral/sublingual DHEA (within 2 days) or testosterone (within 1 day) therapy:** May significantly raise DHEA metabolites (DHEA-S (DHEA therapy only, not T therapy), Etiocholanolone, Androsterone) and testosterone metabolites (Testosterone, 5a-Androstanediol, 5b-Androstanediol) via first-pass effect; Total DHEA Production and testosterone no longer reflect serum levels, but metabolism patterns remain evaluable.
115. **Note on Cushing's:** DHEA may be normal in Cushing's Disease. In some types of Cushing's Syndrome DHEA may even be low. For example, in exogenous Cushing's Syndrome due to glucocorticoid use, glucocorticoid(s) suppress ACTH signaling, and endogenous cortisol/DHEA production.
116. **Low SHBG contributors:** Opioids, androgens, hypothyroidism, nephrotic syndrome, acromegaly, obesity (insulin resistance), PCOS, Cushing's disease,glucocorticoids.
117. **Timing of collection:** Early or late luteal (not mid-luteal) collection. If samples are collected too soon after ovulation, or just before the next period, progesterone may be below (or at the low end) of the luteal range. Mid-luteal collections are ideal, and when accomplished patients will start their period 4-10 days after collection.

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