

DUTCH October FDN Webinar

Case Study on Prescribing Estrogen and Progesterone in a Postmenopausal Woman

Kelly Ruef, ND

Clinical Consultant, Precision Analytical Inc.



Kelly Ruef, ND

Clinical Consultant – Precision Analytical Inc.

Instagram



drkellyhead
Dr. Kelly Head, ND



Female mid-50's

Hot flashes

Vaginal dryness

Insomnia

Fatigue

“Susan”





“Susan”

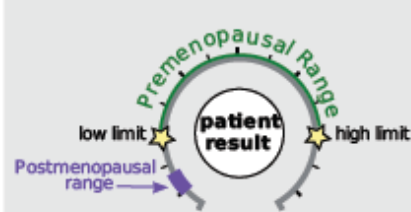
Female mid-50's

- BMI 24
 - Normal range is 18.5-24.9
- High cholesterol
 - Taking Rosuvastatin 5mg daily
- No period x 13 months!

DUTCH Complete Summary: Page #1

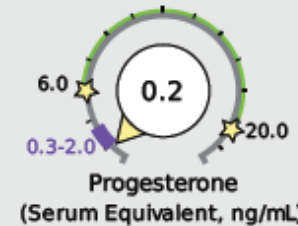
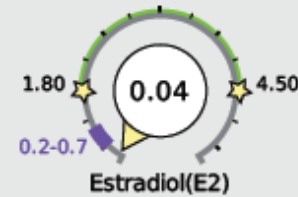
Hormone Testing Summary

Key (how to read the results):



Sex Hormones

See Pages 2 and 3 for a thorough breakdown of sex hormone metabolites

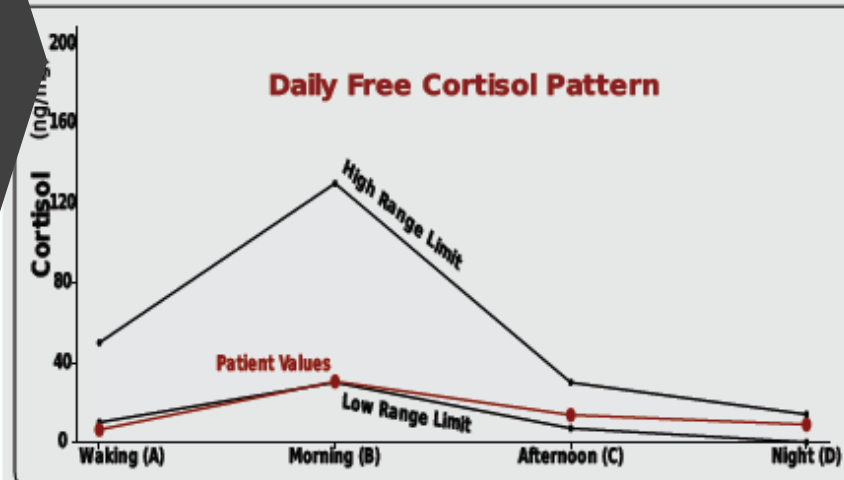


Progesterone Serum Equivalent is a calculated value based on urine pregnanediol.



Adrenal Hormones

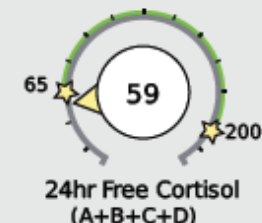
See pages 4 and 5 for a more complete breakdown of adrenal hormones



Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.

Total DHEA Production

Age	Range
20-39	1300-3000
40-60	750-2000
>60	500-1200



cortisol
metabolism

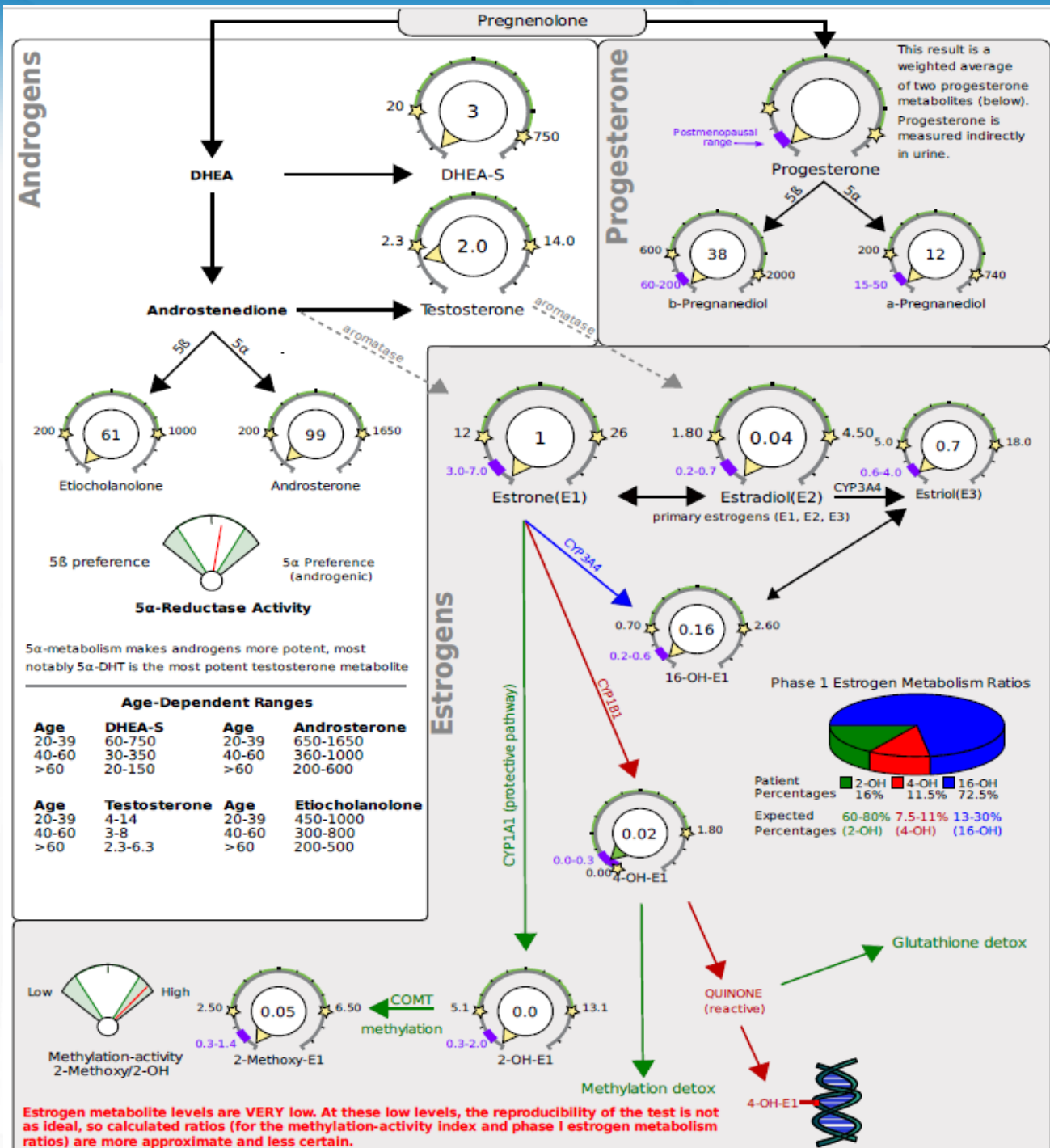


The following videos (which can also be found on the website under the listed names along with others) may aid your understanding:

[DUTCH Complete Overview](#) [Estrogen Tutorial](#) [Female Androgen Tutorial](#) [Cortisol Tutorial](#)

PLEASE BE SURE TO READ BELOW FOR ANY SPECIFIC LAB COMMENTS. More detailed comments can be found on page 7.

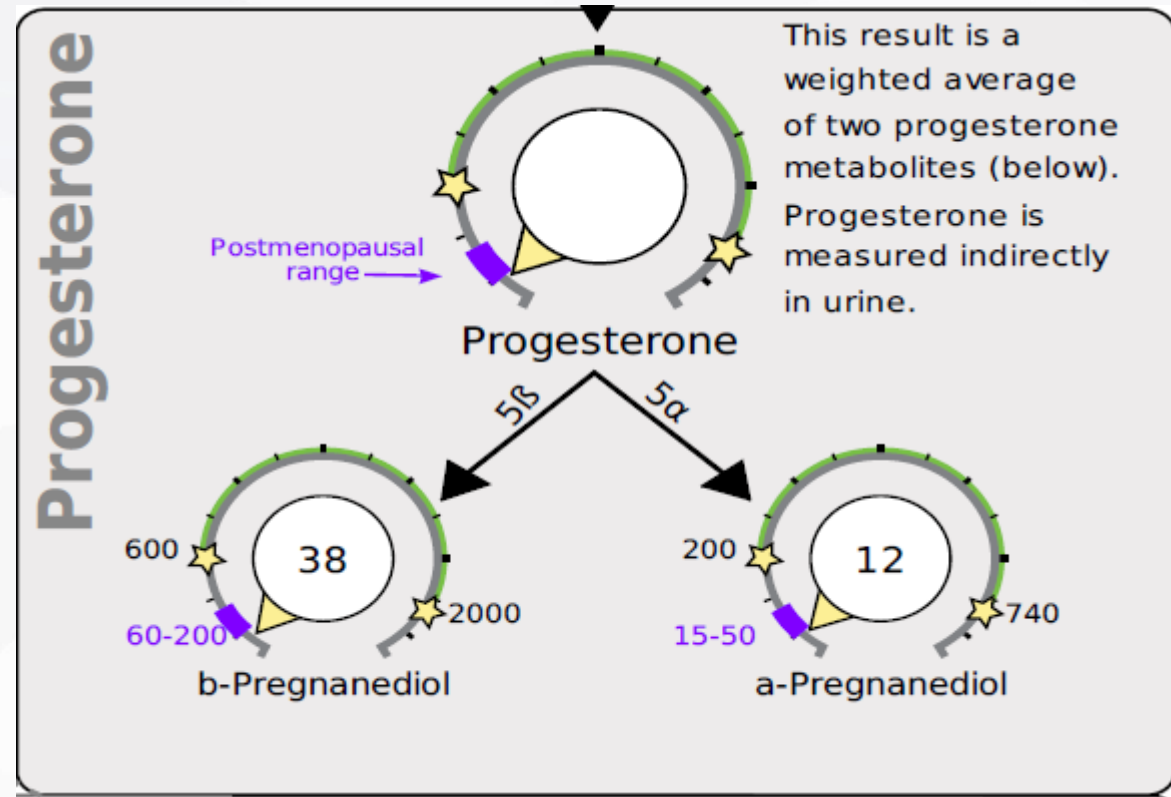
DUTCH Complete Sex Hormones: Page #3



**Let's look at her
progesterone!**

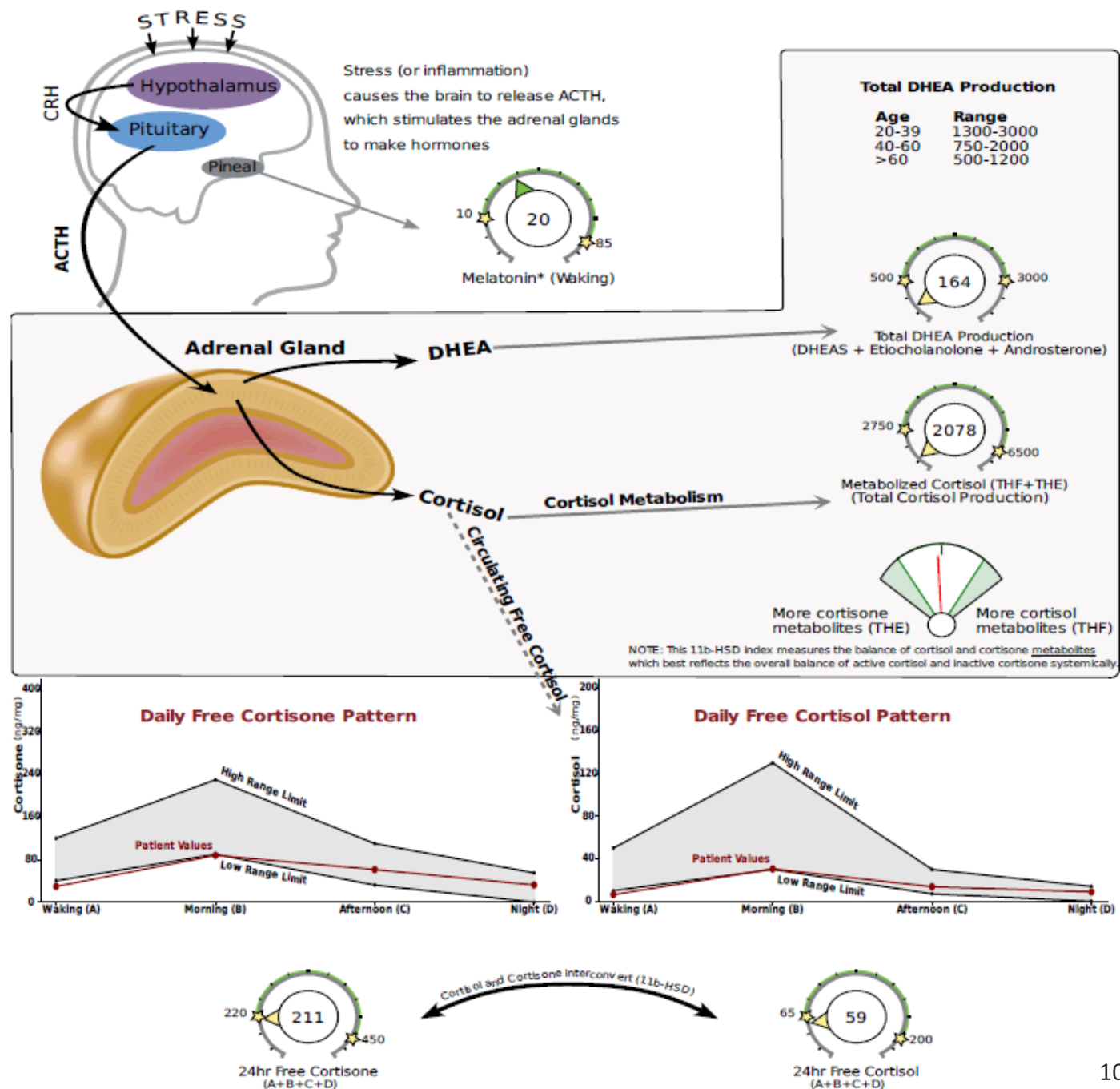
**Progesterone below
the postmenopausal
range**

**Low progesterone in a
postmenopausal
woman is likely due to
low adrenal output.**



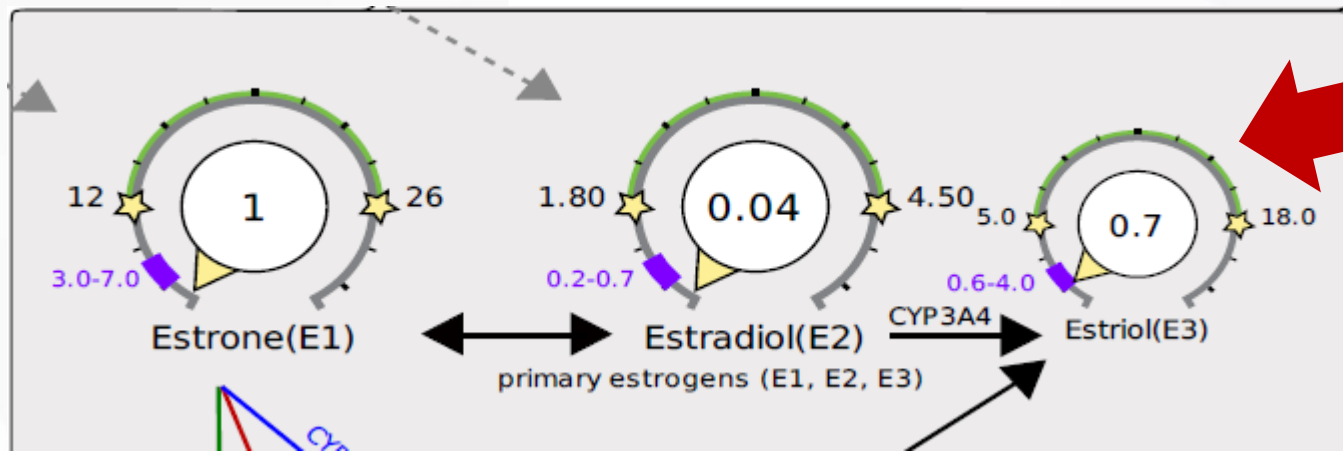
Let's look at her adrenals!

DUTCH Complete Adrenals: Page #5

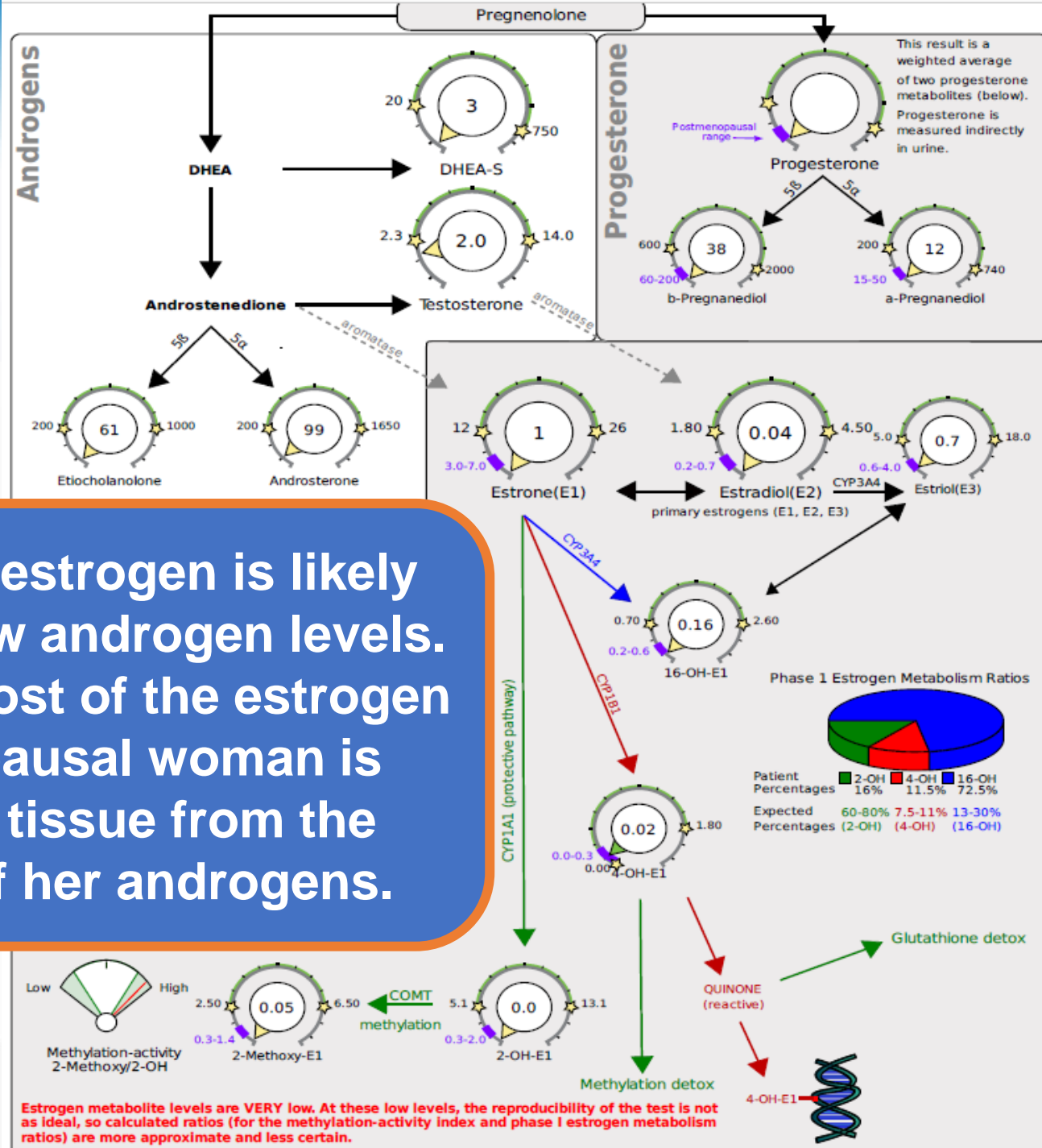


**Let's look at her
estrogen (E1, E2, E3)!**

**E1 and E2 below the
postmenopausal range**



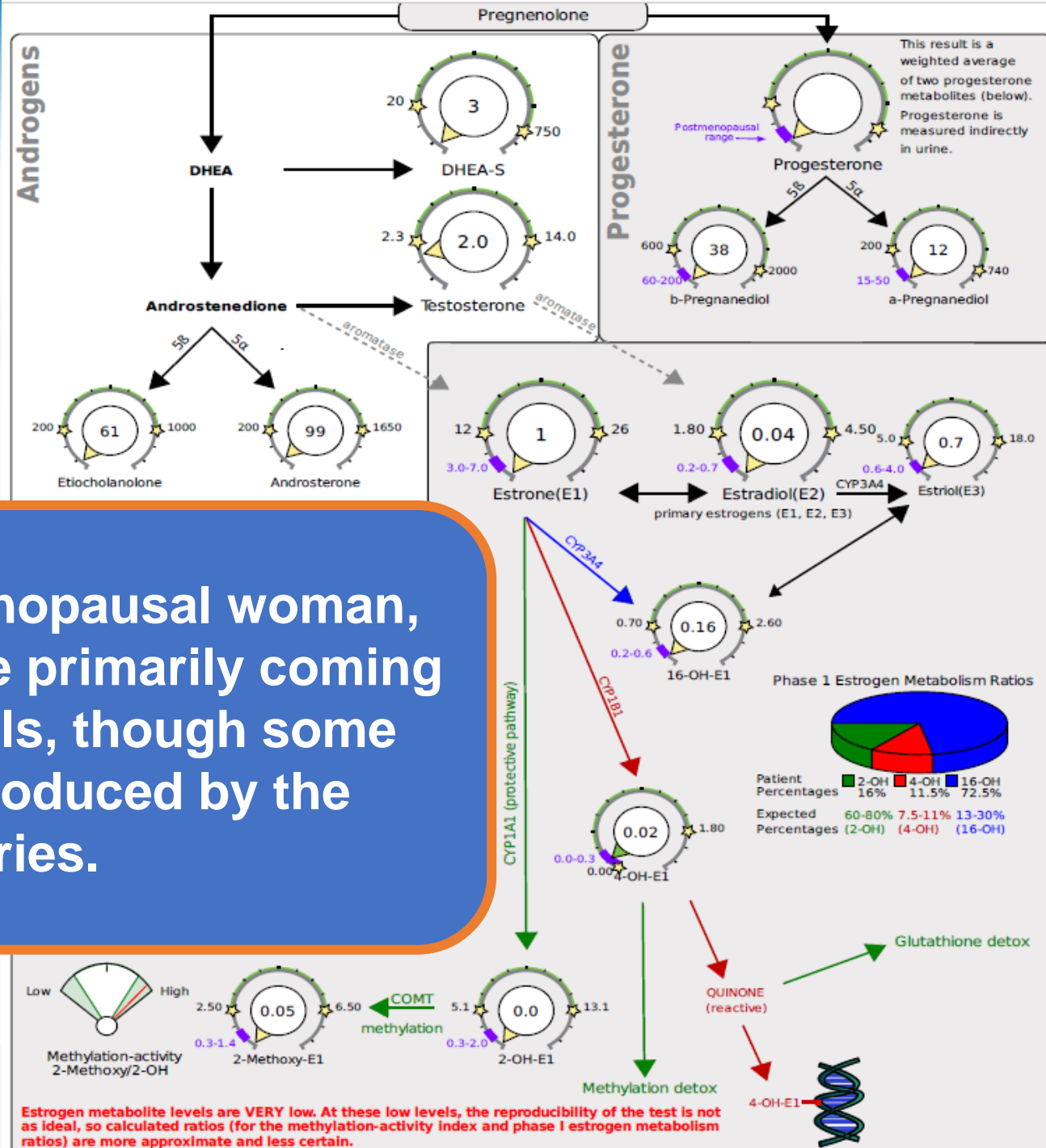
**E3 at the low end of the
postmenopausal range.
Remember that E2 is
metabolized to E3 in the
liver via CYP3A4**



Her below range estrogen is likely due to her very low androgen levels. Remember that most of the estrogen in a postmenopausal woman is made in her fat tissue from the aromatization of her androgens.

Estrogen metabolite levels are VERY low. At these low levels, the reproducibility of the test is not as ideal, so calculated ratios (for the methylation-activity index and phase I estrogen metabolism ratios) are more approximate and less certain.

All rights reserved © 2021 Precision Analytical Inc.

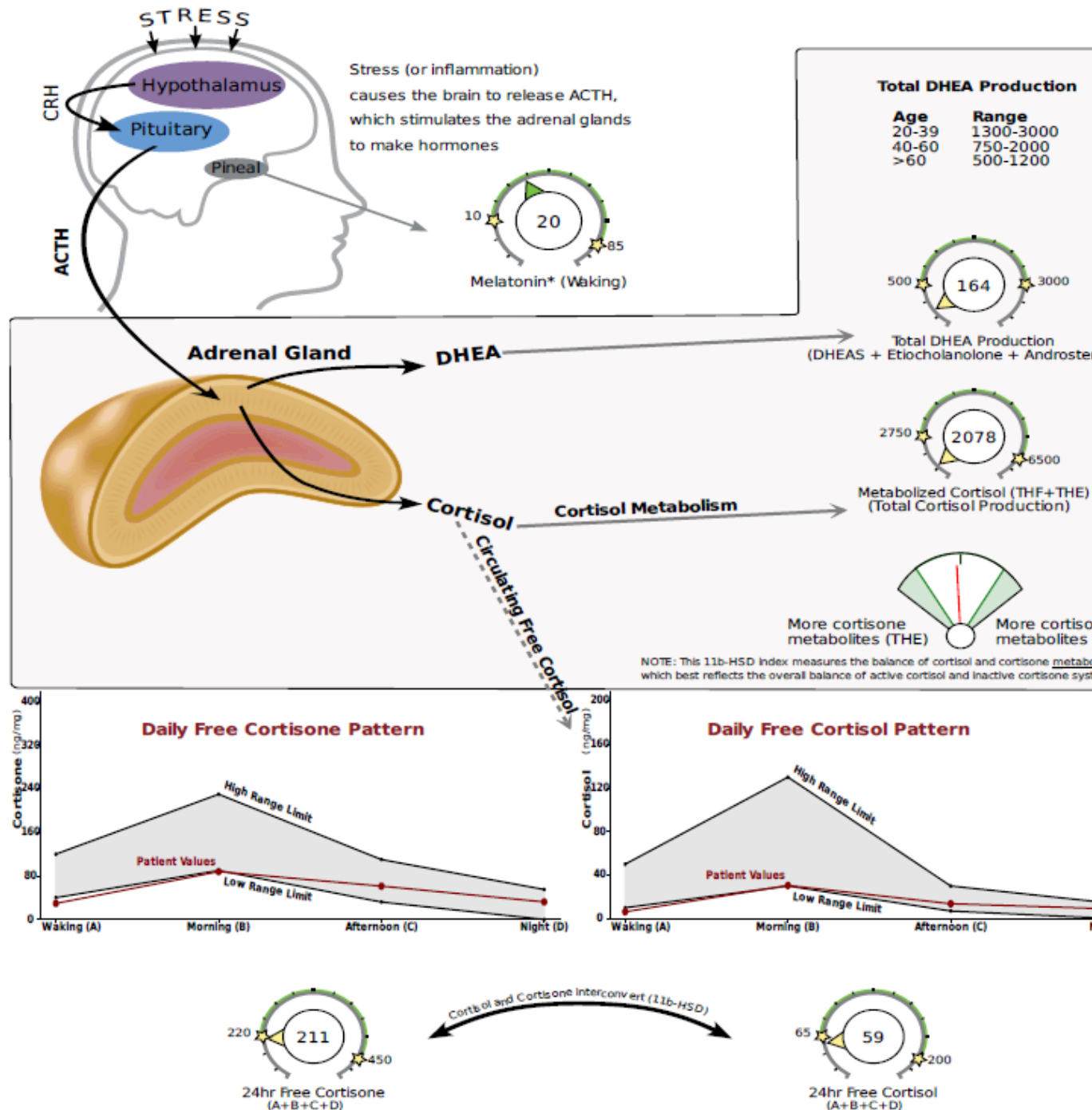


And in a postmenopausal woman, her androgens are primarily coming from her adrenals, though some may still be produced by the ovaries.

DUTCH Complete Adrenals:

Page #5

All rights reserved © 2021 Precision Analytical Inc.



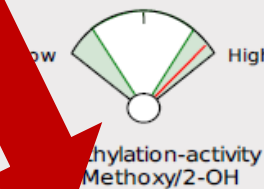
Thus, low adrenal output can lead to low androgen production from the adrenals.

Less androgens in a postmenopausal woman = less to aromatize to estrogen in the fat tissue = lower estrogen levels.

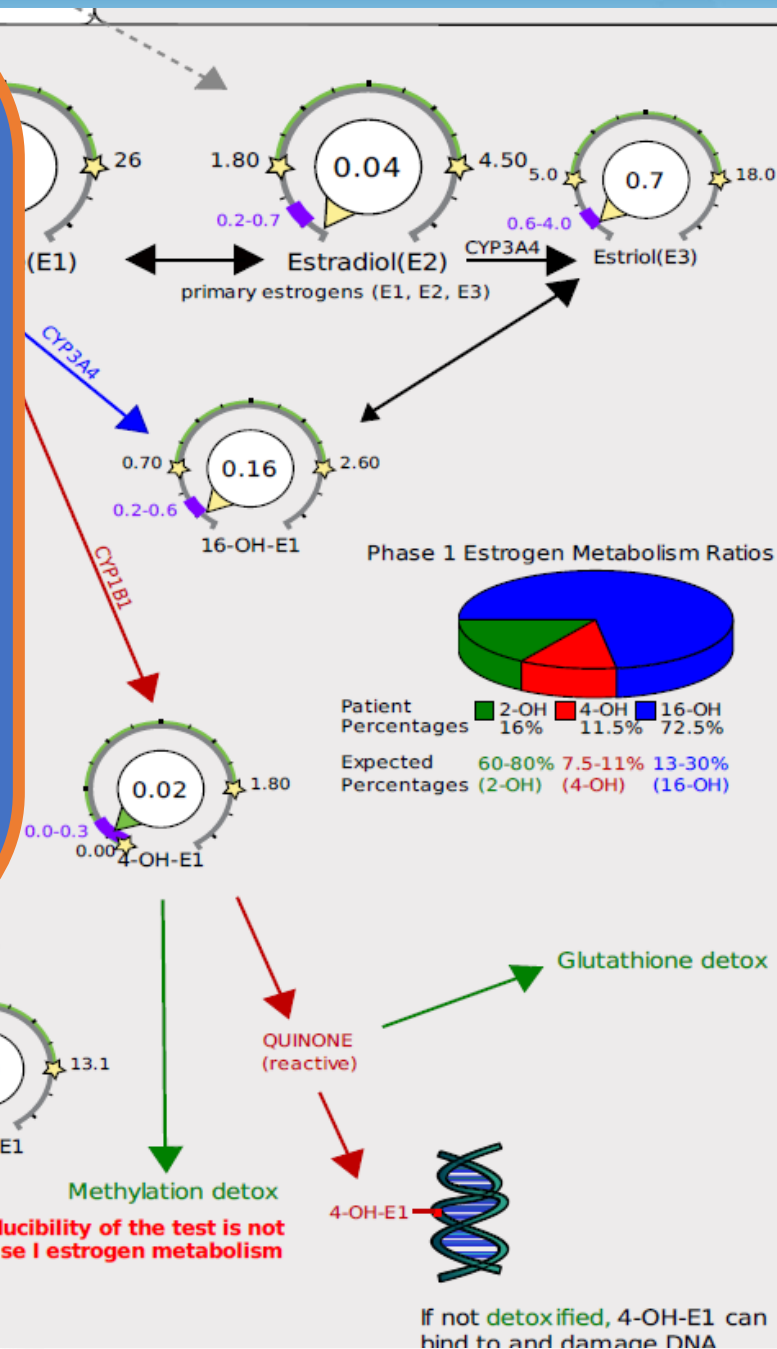
Let's look at her estrogen metabolism patterns!

Please Note:

When you see this red sentence on the bottom of page #3, read it. It says that since estrogen metabolites are very low, the pie chart % and methylation activity index are more of an approximation.



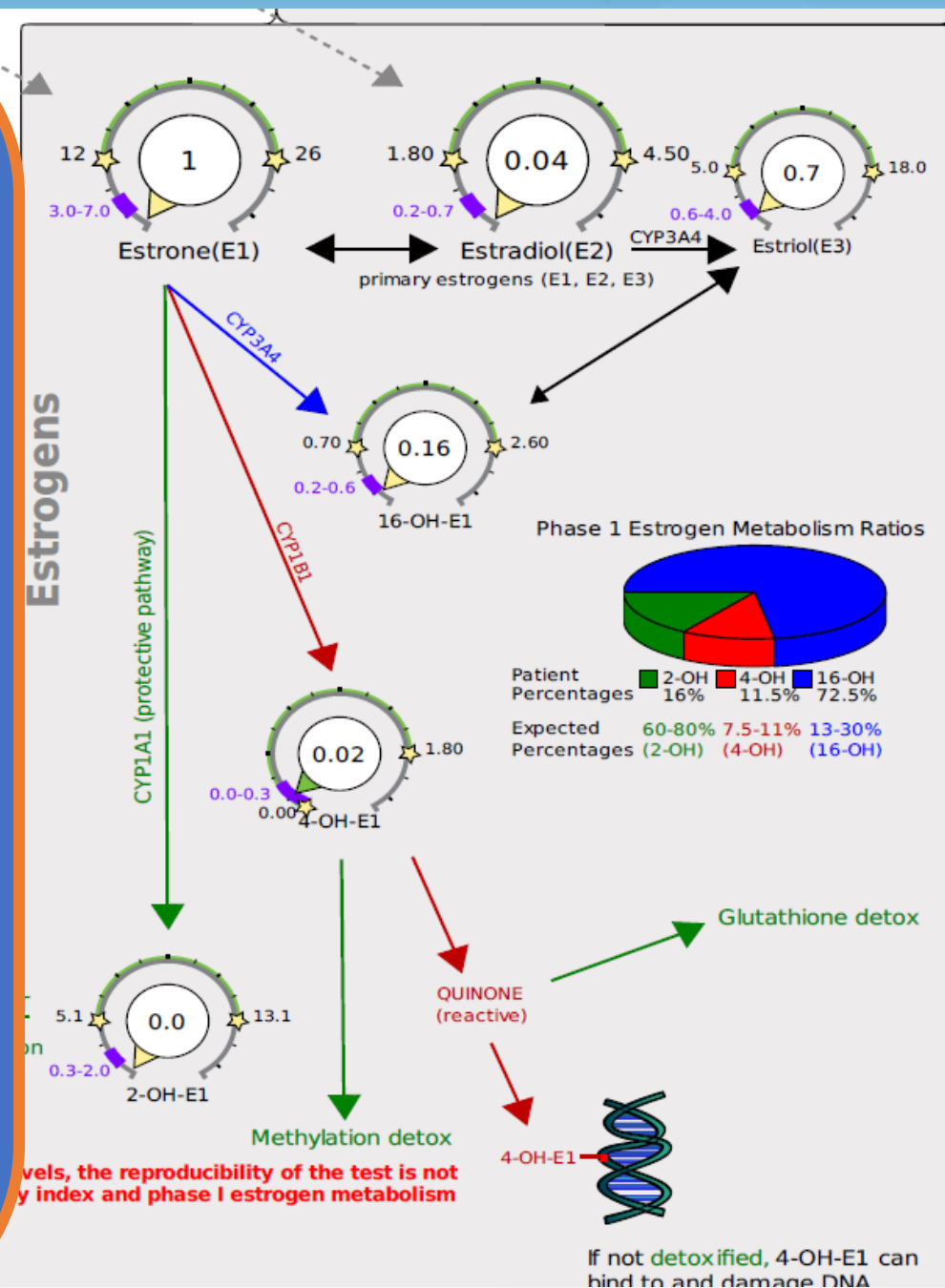
Estrogen metabolite levels are VERY low. At these low levels, the reproducibility of the test is not as ideal, so calculated ratios (for the methylation-activity index and phase I estrogen metabolism ratios) are more approximate and less certain.



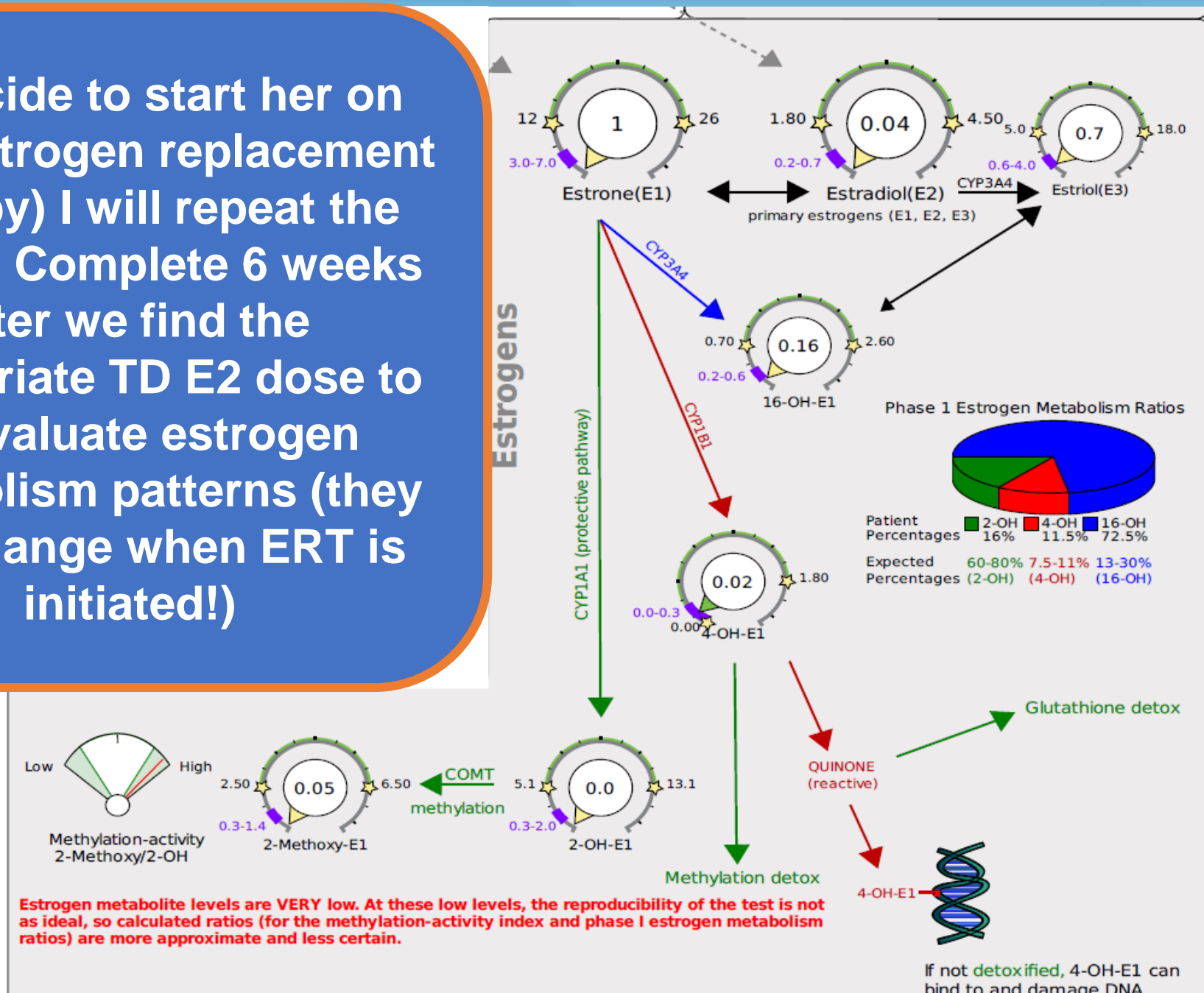
16-OH-E1 (0.16 ng/mg) and 4-OH-E1 (0.02 ng/mg) are below and at the lower end of the postmenopausal range, respectively.

Although the % in the pie chart are elevated, the actual levels are LOW because E1 and E2 are LOW.

Thus, we do not have to worry about elevated 16-OH-E1 or 4-OH-E1 metabolites in this woman if her estrogen continues to be LOW.

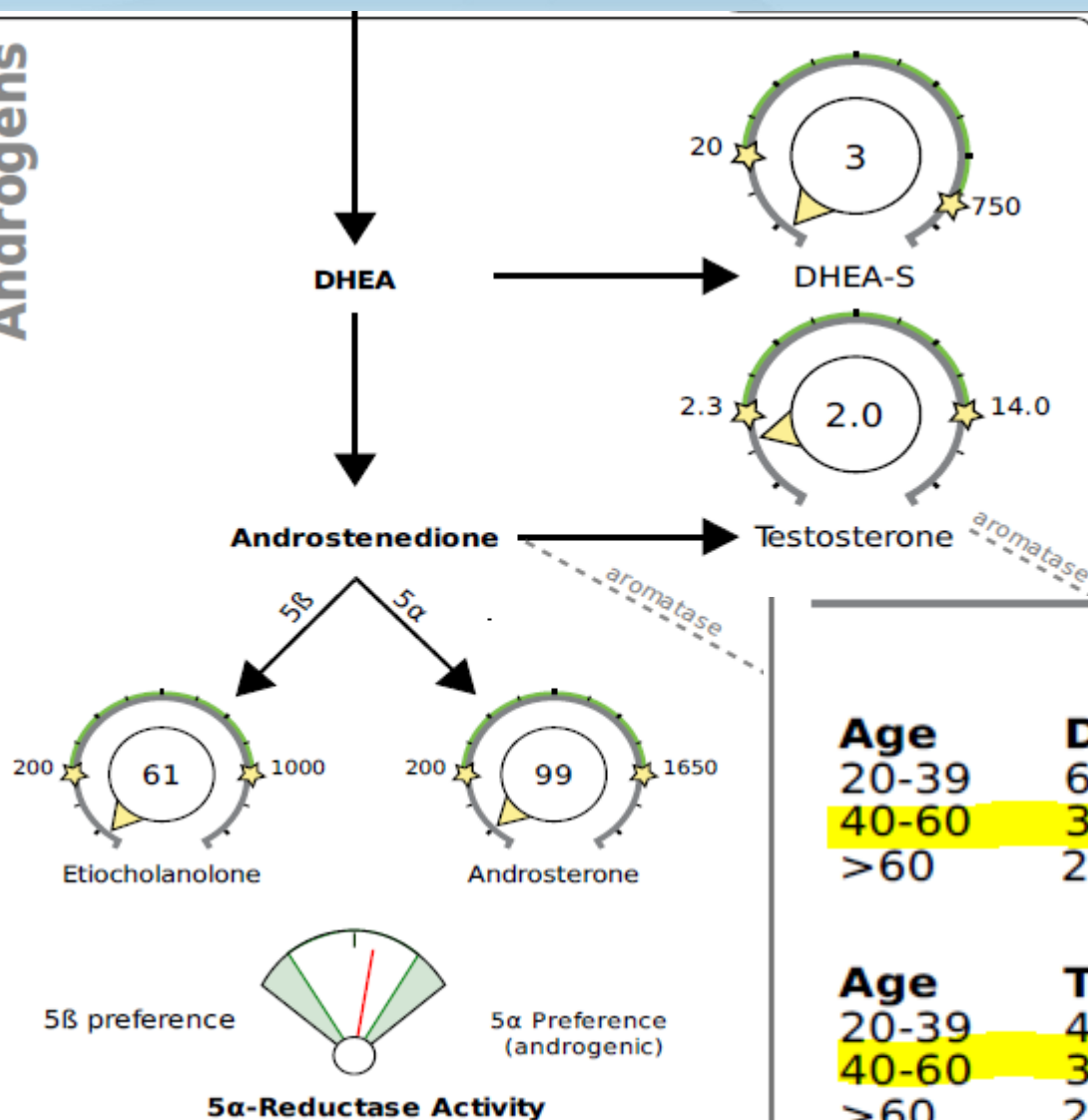


If I decide to start her on ERT (estrogen replacement therapy) I will repeat the DUTCH Complete 6 weeks after we find the appropriate TD E2 dose to re-evaluate estrogen metabolism patterns (they can change when ERT is initiated!)



**Let's look at her
androgens!**

Androgens



All are below range for any age!

Age-Dependent Ranges

Age	DHEA-S	Age	Androsterone
20-39	60-750	20-39	650-1650
40-60	30-350	40-60	360-1000
>60	20-150	>60	200-600

Age	Testosterone	Age	Etiocholanolone
20-39	4-14	20-39	450-1000
40-60	3-8	40-60	300-800
>60	2.3-6.3	>60	200-500

Page #2 Androgens

5a-DHT	Low end of range	0.3	ng/mg	0 - 6.6
5a-Androstenediol	Below range	3.7	ng/mg	12 - 30
5b-Androstenediol	Below range	4.3	ng/mg	20 - 75
Epi-Testosterone	Below range	0.4	ng/mg	2.3 - 14

- Page #2 androgens are all below range.
- Remember 5a-DHT is our most potent androgen.
 - 5a-DHT is 3x more potent/androgenic than testosterone!
 - 5a-androstenediol may be a better indicator of 5a-DHT activity in the cells/tissues than 5a-DHT itself.

Let's look at her OATs page!

DUTCH Complete OATs: Page #6

Category	Test	Result	Units	Normal Range
Nutritional Organic Acids				
Vitamin B12 Marker (may be deficient if high) - (Urine)				
	Methylmalonate (MMA)	Within range	1.6	ug/mg 0 - 2.5
Vitamin B6 Markers (may be deficient if high) - (Urine)				
	Xanthurenate	Within range	0.56	ug/mg 0.12 - 1.2
	Kynurenate	Within range	2.9	ug/mg 0.8 - 4.5
Glutathione Marker (may be deficient if low or high) - (Urine)				
	Pyroglutamate	Within range	38.5	ug/mg 28 - 58
Neurotransmitter Metabolites				
Dopamine Metabolite - (Urine)				
	Homovanillate (HVA)	Within range	8.9	ug/mg 3 - 11
Norepinephrine/Epinephrine Metabolite - (Urine)				
	Vanilmandelate (VMA)	Within range	4.8	ug/mg 2.2 - 5.5
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)				
	Melatonin* (Waking)	Low end of range	20.4	ng/mg 10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)				
	8-OHdG (Waking)	Within range	2.3	ng/mg 0 - 5.2

Let's talk about MHT!

MHT = menopausal hormone therapy



Her progesterone is BELOW
the postmenopausal range

Her estrogen is BELOW the
postmenopausal range



She obviously has symptoms of low estrogen and low progesterone:

Hot flashes, vaginal dryness, insomnia, fatigue



So, should we start her on MHT?

MHT = menopausal hormone therapy



Maybe?!



We don't know until we do further workup to determine:

- Treatment goals
- Relative risks of using MHT
- Patient's preferences



Before Starting MHT

Contraindications

- Estrogen dependent cancer (endometrial CA, even lung cancers with ERB and Era receptors!)
- Suspected or known breast cancer
- Abnormal genital bleeding
- Active liver disease
- Transient ischemic attack (TIA)
- Venous thromboembolic disease (DVTs, PE)
- Consider using caution with migraines (especially with aura), gallbladder disease, etc.



Before Starting MHT

Mammogram, PAP & Pelvic Exam

- To rule out malignancy & any abnormal findings
- Document these findings in your EHR!!!

Before Starting MHT

- “We conclude that HRT for prevention of osteoporosis and cardiovascular disease should be administered in a menopausal clinic by a gynecologist, after performing a few tests: **confirmation of menopause by follicle-stimulation hormone (FSH) and E2, excluding malignancy by mammography, and confirmation of normal lipid metabolism.**”

Pardo J, Kaplan B, Neri A, Blum M. Clinical and laboratory work-up prior to hormone replacement therapy in postmenopausal women. Clin Exp Obstet Gynecol. 1992;19(4):215-7. PMID: 1294340.

Before Starting MHT

- Basic labs
 - CBC (complete blood count)
 - CMP (comprehensive metabolic panel)
- Blood sugar
 - Fasting glucose (usually included in CMP; <85 ideal)
 - Fasting insulin (<10 ideal)
 - HbA1c





Before Starting MHT

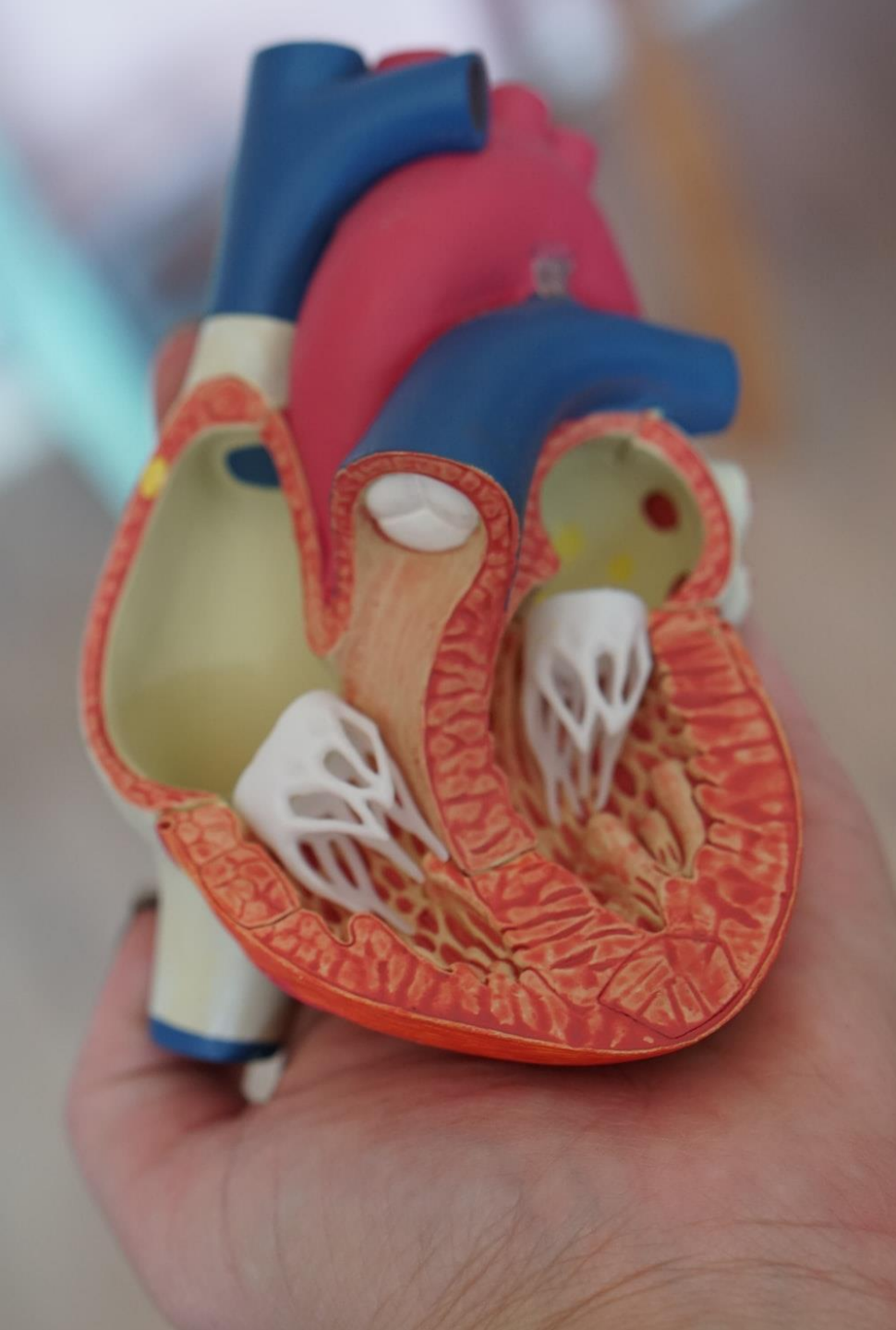
Cardiovascular markers

- Total cholesterol, LDL-P (<1000 ideal), ox-LDL (<60 U/L ideal), HDL, triglycerides, APO-B (<60 ideal), TMAO (< 6.2 μ M ideal), hs-CRP (<1.0 ideal)
- Coronary calcium scan (0 score ideal; 100-300 moderate plaque deposits and high risk; >300 severe risk of heart attack or other heart disease over the next 3-5 years)
- Graded exercise stress test (GXT)

Cardiovascular Disease

“For women at moderate risk of cardiovascular disease (CVD; 5 to 10 percent 10-year risk), we suggest transdermal rather than oral estrogen. For women with a uterus, we suggest micronized progesterone rather than synthetic progestins such as medroxyprogesterone acetate (MPA).”

Martin KA et. al. Treatment of menopausal symptoms with hormone therapy. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 05, 2021.)



Cardiovascular Disease

Evaluating CVD risk in women contemplating MHT

10-year CVD risk	Years since menopause onset
	<10 years
Low (<5%)	MHT ok
Moderate (5 to 10%)	MHT ok (choose transdermal)
High (>10%)*	Avoid MHT

* High risk includes known myocardial infarction (MI), stroke, peripheral artery disease, etc.

Calculate 10-year risk of heart disease or stroke:
<http://www.cvriskcalculator.com/>

Martin KA et. al. Treatment of menopausal symptoms with hormone therapy. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 05, 2021.)

What About Oral Estrogens?

STOP

Oral E and o-E2 undergo extensive first-pass intestinal and hepatic metabolism. This results in protein production, including inflammatory proteins and binding proteins. All o-E's, because of increased clotting factors, **increase thromboembolic risk**. In contrast, TD E2, at commonly used doses, exerts minimal effects on inflammatory proteins, clotting factors, and/or binding proteins. TD E2 is a safer alternative to any o-E, including o-E2.⁶⁻⁸

STOP

NOTE: *This material is educational and not an endorsement for a particular HRT dose or route of administration.*

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

Before Starting MHT

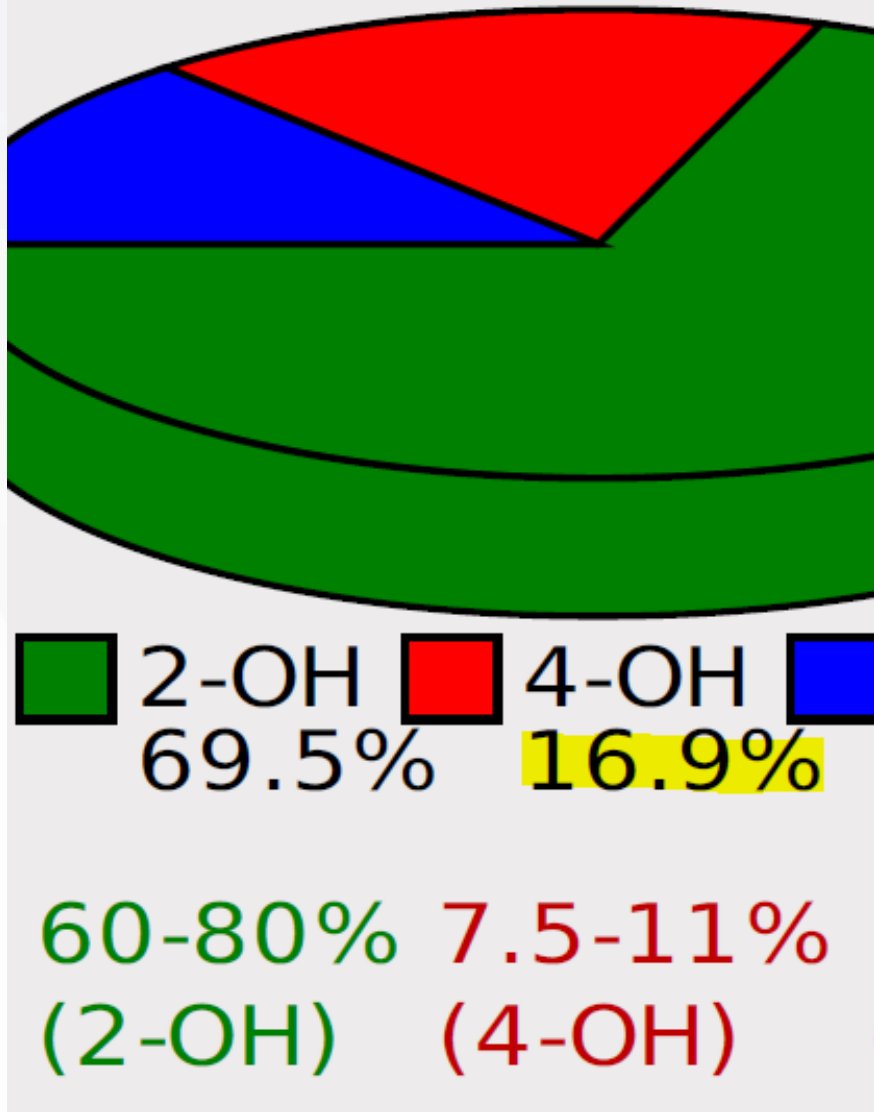
- Hormone markers

- Thyroid (TSH, fT3, fT4, rT3, TPO ab, thyroglobulin Ab)
- Vitamin D
- Prolactin, LH, FSH (to confirm menopause)
- E2, Pg, total T, DHEA-S, SHBG***

***Make sure to test sex hormones using high sensitivity testing methods (LC-MS/MS). High sensitivity testing is needed to best evaluate the **low** hormone levels seen in postmenopausal women!



Estrogen Metabo



Before Starting MHT

Hormone metabolism patterns and adrenal Health

- Look at DUTCH Complete or DUTCH Plus
- Favoring the CYP1B1 pathway towards 4-OH metabolites (increased risk for breast cancer)?
- Favoring the alpha (5 α -reductase) pathway for the androgens and progesterone?
- Cortisol diurnal curve and total cortisol output look good?

Before Starting MHT

Assess breast cancer risk


- ***“Breast cancer remains the second leading cause of cancer death among women overall and the leading cause of cancer death among Hispanic women.”*** – Centers for Disease Control and Prevention



Factors Associated with Greater Breast Cancer Risk

MHT (Menopausal Hormone Therapy)?

- Increased breast density is an independent risk factor for breast cancer
- High mammographic density increases breast cancer risk four- to six-fold
- E2 does not increase breast density
- E/E2, and TD E2-alone, are associated with a decreased breast cancer mortality
- TD E2 + OMP does not increase breast cancer



Saltiel, Doreen. *DUTCH Test* (2020): *TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

NOTE: This material is educational and not an endorsement for a particular HRT dose or route of administration.

Factors Associated with Greater Breast Cancer Risk

MHT (Menopausal Hormone Therapy)?

The four concerns raised by the Women's Health Initiative publications (venous thromboembolic disease, myocardial infarction, stroke, and breast cancer) are minimized or negated by using TD E2 and OMP or VMP. Therefore, there is no role for any synthetic estrogen or progestin.

Saltiel, Doreen. *DUTCH Test* (2020): *Menopausal Hormone Therapy, Breast Cancer, and Mortality: The Same Story on a Different Day*
<https://dutchtest.com/2020/10/19/menopausal-hormone-therapy-breast-cancer-and-mortality-the-same-story-on-a-different-day/>

NOTE: This material is educational and not an endorsement for a particular HRT dose or route of administration.

Factors Associated with Greater Breast Cancer Risk



REMEMBER: many other factors increase a woman's risk for breast cancer so we cannot forget about assessing these!



Factors Associated with Greater Breast Cancer Risk

Personal history of breast cancer?

- “A personal history of either invasive or in situ breast cancer increases the risk of developing an invasive breast cancer in the contralateral breast.”

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)



Factors Associated with Greater Breast Cancer Risk

Family history of breast cancer?

- “Increased almost twofold if a woman had one affected first-degree relative.”
- “Increased threefold if she had two affected first-degree relatives.”
- The **age at diagnosis** of the affected first-degree relative also influences the risk for breast cancer. Women have a threefold higher risk if the first-degree relative was diagnosed before age 30 [...] but the risk is only 1.5-fold higher if the affected relative was diagnosed after age 60.”



Factors Associated with Greater Breast Cancer Risk

Increasing age

- Birth to age 49 – 2.1 percent (1 in 49 women)
- Age 50 to 59 – 2.4 percent (1 in 42 women)
- Age 60 to 69 – 3.5 percent (1 in 28 women)
- Age 70 and older – 7.0 percent (1 in 14 women)
- Birth to death – 12.9 percent (1 in 8 women)

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)

Factors Associated with Greater Breast Cancer Risk

Female Sex

“Breast cancer occurs **100 times more frequently in women than in men**. In the United States, over 280,000 women are diagnosed with invasive breast cancer each year, compared with fewer than 3000 cases that occur annually in men”



Factors Associated with Greater Breast Cancer Risk

White Race

“...the rate of newly diagnosed breast cancer (per 100,000 women) was 124 and 122 for White and Black women, respectively. Despite this, Black women ...had a 41 percent higher breast cancer-specific mortality rate (30 versus 21 deaths per 100,000 women).”





Factors Associated with Greater Breast Cancer Risk

BMI (Body Mass Index)

- Postmenopausal women:
 - “A higher BMI and/or perimenopausal weight gain have been consistently associated with a higher risk of breast cancer among postmenopausal women.”
- Premenopausal women:
 - “Unlike postmenopausal women, an increased BMI is associated with a **lower** risk of breast cancer in premenopausal women, particularly in early adulthood”

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)

Factors Associated with Greater Breast Cancer Risk

Tall Stature

- “Increased height is associated with a higher risk of breast cancer in both premenopausal and postmenopausal women. In one study, women who were >175 cm (69 inches) tall were 20 percent more likely to develop breast cancer than those <160 cm (63 inches) tall.”

69" = 5' 9"

63" = 5' 3"

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)



Factors Associated with Greater Breast Cancer Risk

Benign breast disease

- “...proliferative lesions (especially those with histologic atypia) are associated with an increased risk of breast cancer.”

Dense breast tissue

- “generally defined as dense tissue comprising ≥ 75 percent of the breast.”



All rights reserved © 2021 Precision Analytical Inc.



Factors Associated with Greater Breast Cancer Risk

BMD (Bone Mineral Density)

- “Because bone contains ERs [estrogen receptors] and is highly sensitive to circulating estrogen levels, bone mineral density (BMD) is considered a surrogate for long-term exposure to endogenous and exogenous estrogen.”

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)



Factors Associated with Greater Breast Cancer Risk

Higher Endogenous Estrogen Levels

- “Higher endogenous estrogen levels are associated with higher breast cancer risk (particularly hormone receptor-positive disease) in both postmenopausal and premenopausal women.”



Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)

Factors Associated with Greater Breast Cancer Risk

OCPs (Oral Contraceptives)

- “Breast cancer risk is temporarily increased with current or recent use of combined oral contraceptives, but this association disappeared within two to five years of discontinuation.”





Factors Associated with Greater Breast Cancer Risk

Androgens?

- “Preclinical data suggest that androgens (in particular, testosterone) exert dual effects on mammary tumor development, with a **proliferative effect mediated by the ER and an antiproliferative effect mediated by the androgen receptor.**”
- “**Testosterone association with breast cancer subtypes has not been consistently seen.** Some studies suggest that elevated testosterone levels increase the risk of breast cancer specifically for hormone receptor-positive breast cancers, while one study suggests elevated testosterone levels are associated with a lower risk of hormone receptor-negative breast cancers.”

Factors Associated with Greater Breast Cancer Risk

Insulin Resistance

- “In reports from the Women's Health Initiative, higher insulin resistance levels were associated with higher breast cancer incidence.”



Factors Associated with Greater Breast Cancer Risk

Earlier Menarche or Later Menopause

- “Women with menarche at or after 15 years of age were less likely to develop hormone receptor-positive breast cancer compared with women who experienced menarche before the age of 13 years.”

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)



A pregnant woman with long dark hair, wearing a green button-down shirt, is shown from the waist up. She is holding her belly with both hands. The background is a wooden wall.

Factors Associated with Greater Breast Cancer Risk

Nulliparity (woman who hasn't given birth to a child)

- “Although parous women have an increased risk for developing breast cancer within the first few years of delivery relative to nulliparous women, parity confers a protective effect decades after delivery.”

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)

A close-up photograph of a pregnant woman's belly, which is wrapped in a pink, textured cloth. Several hands are gently touching and supporting her belly. The woman is wearing a gold ring on her finger and a black and white patterned bracelet on her wrist.

Factors Associated with Greater Breast Cancer Risk

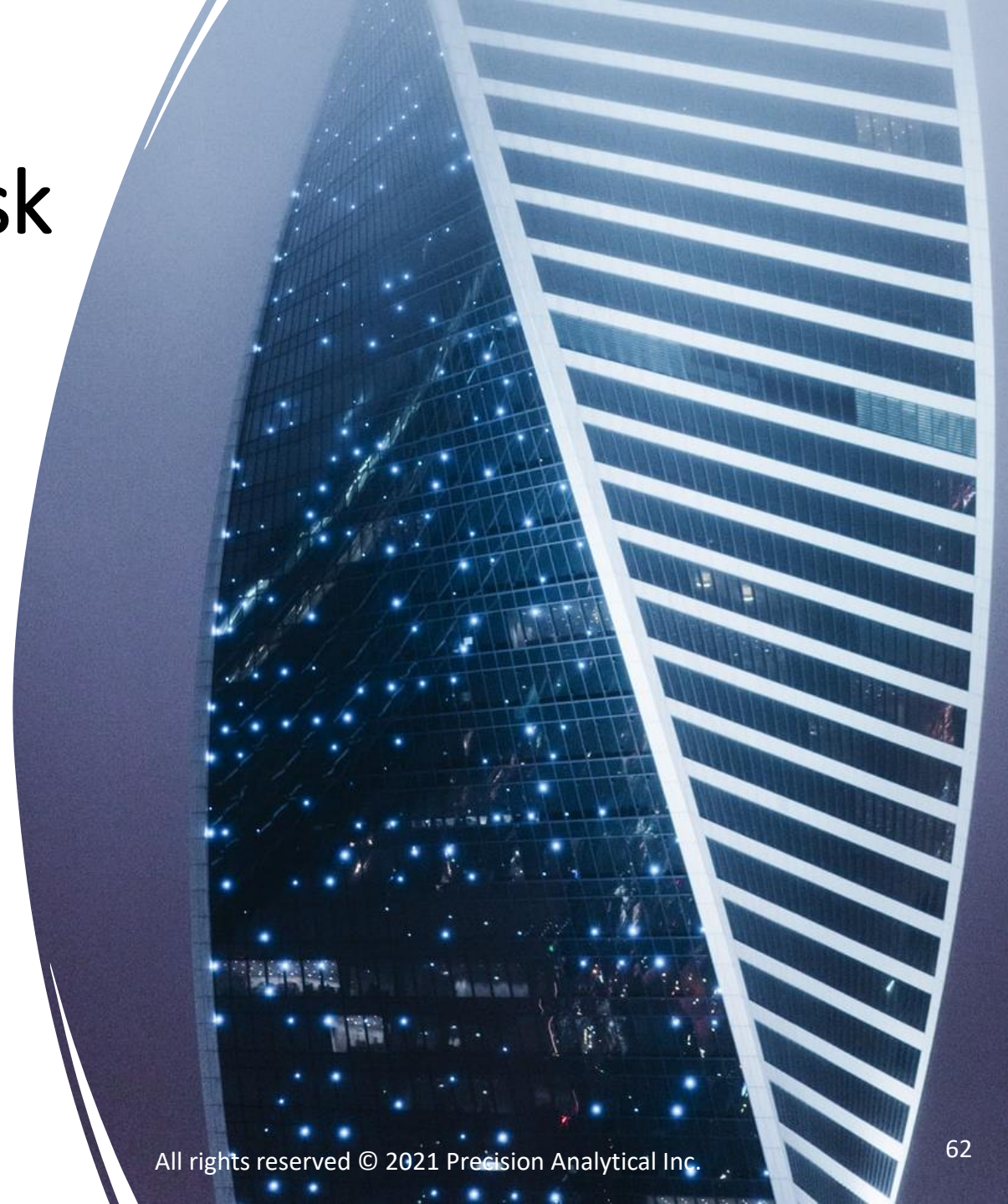
Increasing Age at First Full-Term Pregnancy

- “In the Nurses' Health Study, compared with nulliparous women at or near menopause, the cumulative incidence of breast cancer (up to age 70) was 20 percent lower among women who delivered their first child at age 20; 10 percent lower for those delivering their first child at age 25 years; and 5 percent higher among those delivering their first child at 35 years.”
- “The risk for a nulliparous woman of any age was similar to that of a woman with a first full-term birth at age 35.”

Factors Associated with Greater Breast Cancer Risk

Genetic Mutations

- “Specific genetic mutations that predispose to breast cancer are **rare**; only **5 to 6 percent of all breast cancers are directly attributable to inheritance of genetic mutations**, including *BRCA1*, *BRCA2*, *p53*, *STK11*, *CDH1*, *PALB2*, *PTEN*, and the mismatch repair genes.”





Factors Associated with Greater Breast Cancer Risk

Alcohol and Smoking

- “Alcohol consumption is associated with a higher risk of breast cancer.”
- “Although results have not been uniform, multiple studies suggest there is a modestly increased risk of breast cancer in smokers.”

Chlebowski RT. Factors that modify breast cancer risk in women. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 02, 2021.)

Factors Associated with Greater Breast Cancer Risk

Exposure to Ionizing Radiation

- “Exposure to ionizing radiation of the chest at a young age, as occurs with treatment of Hodgkin lymphoma or in survivors of atomic bomb or nuclear plant accidents, is associated with an increased risk of breast cancer.”
- “The most vulnerable ages appear to be between 10 to 14 years (prepuberty), although excess risk is seen in women exposed as late as 45 years of age. After age 45, risk is attenuated.”



What are some indications for MHT?

MHT = menopausal hormone therapy

Estrogen & Hot Flashes (VMS)

- TD E2 patch doses as low as 0.014mg/d (MENOSTAR) relieve VMS
- TD E2 gel doses as low as 0.25mg/d (DI-VIGEL) and 0.52mg/d (ELESTRIN) relieve VMS (low-dose gels are product specific)
- With lower than standard patch and gel doses it may take longer to see effects
- OMP/VMP should be prescribed, even with lower TD E2 doses

NOTE: This material is educational and not an endorsement for a particular HRT dose or route of administration.

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

Estrogen & Vaginal Atrophy

- TD E2 products relieve VVA symptoms
- TD E2 patch doses as low as 0.014mg/d are effective
- ELESTRIN gel 0.52mg/d and ESTROGEL 0.75mg/d and 0.375mg/d are effective
- The ESTROGEL 0.27mg/d does not provide adequate amounts of E2 to effectively improve VVA symptoms and/or VMI

NOTE: This material is educational and not an endorsement for a particular HRT dose or route of administration.

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

Cardiovascular Disease (CVD)

- TD E2 decreases CVD, with no increase in VTE or stroke
- TD patch doses as low as 0.025mg/d and TD E2 gel doses of 1-2mg/d may decrease CVD mortality risk
- TD E2's mortality reduction is positively related to E2 exposure time
- Know a woman's CVD risk prior to initiating MHT
- CVD risk changes; ongoing surveillance a must

NOTE: *This material is educational and not an endorsement for a particular HRT dose or route of administration.*

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

Cognition

- **ESTRADERM 0.05mg/d and 0.1mg/d** improve cognitive performance in older, healthy PMP women with mild-moderate AD
- **CLIMARA 0.05mg/d** improves cognitive performance in younger, symptomatic, perimenopausal, and recently menopausal women
- MENOSTAR 0.014mg/d does not improve cognitive performance in predominantly asymptomatic, older PMP women.
- A 0.025mg/d TD E2 patch's effectiveness on cognitive performance has yet to be studied

NOTE: *This material is educational and not an endorsement for a particular HRT dose or route of administration.*

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

Estrogen & Bone Mineral Density (BMD)

- TD E2 products improve BMD and are FDA-approved for osteoporosis prevention
- Low-dose (0.025mg/d) CLIMARA, ALO-RA, and ESTRODERM improve BMD vs placebo, as does the ultralow-dose (0.014mg/d) MENOSTAR
- Low-dose TD E2 gels are not FDA-approved for osteoporosis prevention
- Standard-dose ESTROGEL 0.75mg/d improves BMD, but response is delayed (1 year)

NOTE: *This material is educational and not an endorsement for a particular HRT dose or route of administration.*

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

Estrogen & Bone Mineral Density (BMD)

Low dose patches contain 0.4-5.0mg of E2 and deliver 0.025mg of E2 daily. This dose increases bone mineral density (BMD) and improves vasomotor symptoms (VMS), vulvovaginal (VVA) symptoms, and other related symptoms.

Serum or urine levels just outside the postmenopausal range and up to the lower limit of the premenopausal (luteal) range may be optimal targets for both E2 patches and gels. Serum, 20-60pg/mL; DUTCH, 0.7-1.8ng/mg.

NOTE: *This material is educational and not an endorsement for a particular HRT dose or route of administration.*

Mark, Newman. *DUTCH Test (2019): TRANSDERMAL (TD) ESTRADIOL (E2) A Critical Review of the Literature and Available Data.*
<https://dutchtest.com/wp-content/uploads/2020/07/TD-E2-Lab-Ref062620.pdf>

What About Compounded E2 Creams?

WHAT ABOUT COMPOUNDED TD E2 CREAMS?

While TD E2 patches and gels have been proven to be effective, there are **presently no outcome studies** evaluating compounded products, including TD E2 creams. While they may be effective, there is no data on dosing, laboratory findings, and/or clinical success.

NOTE: *This material is educational and not an endorsement for a particular HRT dose or route of administration.*

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

**Remember to protect the
uterus with progesterone
if using ERT!!!**

ERT = Estrogen Replacement Therapy

Protecting the Uterus

- Unopposed TD E2 increases endometrial hyperplasia and cancer risk
- PROMETRIUM 200mg, either continuous or sequential (12-14 days), with standard-dose CLIMARA 0.05mg/d, is proven to prevent endometrial cancer
- There is a paucity of long-term follow-up data and/or RCT data on lower TD E2 and OMP doses and regimens

NOTE: This material is educational and not an endorsement for a particular HRT dose or route of administration.

Saltiel, Doreen. *DUTCH Test (2020): TRANSDERMAL ESTRADIOL'S USE IN MENOPAUSE: An Evidence-Based Affirmation*
<https://dutchtest.com/wp-content/uploads/2020/11/TD-E2-Clinical-Ref092820.pdf>

Protecting the Uterus

From Dr. Doreen Saltiel's recent DUTCH Webinar on MHT
dutchtest.com/video/menopausal-hormone-therapy-clinical-benefits-and-outcome-studies

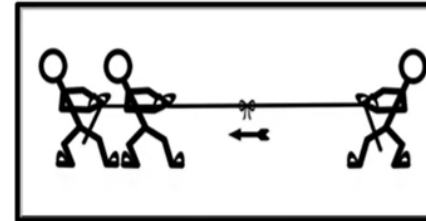
TD Pg: Not Recommended for Endometrial Protection

TD Pg is NOT Protective

- **Wren (2000) 3-month pilot study**
 - Determine TD Pg's endometrial effects
 - TD E2 0.1mg/d patch w/ either: TD Pg 16, 32, or 64mg x 14 days
 - No endometrial protection, No progestogenic effect
 - Saliva levels way exceeded serum luteal levels, with no endometrial effect
- **Vashisht (2005) 4-year open study**
 - TD Pg's endometrial effects
 - Oestrogel 1mg/d + TD Pg 40mg/d continuously
 - 32% endometrial proliferation or hyperplasia

TD Pg is Protective

- **Leonetti (2005) 1-year RCT**
 - Determine TD Pg's endometrial effects
 - TD Pg 20mg BID added to CEE 0.625mg/d protects the endometrium
 - Results are encouraging
 - "Although the lack of endometrial hyperplasia is promising, additional longer clinical trials to ensure safety are required before transdermal PC can be offered as an alternative to standard HRT."



NOTE: This material is educational and not an endorsement for a particular HRT dose or route of administration.

Oral Progesterone for Sleep and Anxiety

- Keep in mind that the **alpha progesterone metabolites act on the GABA receptors in the brain!**
- Oral Pg leads to the highest increase in progesterone metabolites, as 90% of it gets metabolized right away during 1st pass metabolism in the gut and liver.
- This is why oral Pg is taken before bed – it tends to make women groggy and sleepy!
- Oral Pg can also help with mood (GABA support) 😊

Treatment Considerations



Note that treatment (and possibly further workup) will depend upon test results. **We MUST treat the cause!** 😊

Example Treatment Plan: MHT

- **TD Estradiol Patch 0.025**
 - To help with hot flashes, vaginal dryness, insomnia, mood issues, BMD, cardiovascular system, cognition
- **Oral Progesterone 100mg qhs**
 - To improve sleep & anxiety (increases alpha progesterone metabolites that act on GABA receptors). May improve hot flashes in some women.
 - To protect her uterus from endometrial hyperplasia
- **Oral DHEA 5mg TID and TD T Cream 1.0 mg/g (SIG: apply 1 mg daily)**
 - To help with fatigue, mood issues, BMD, cardiovascular system
- **Vaginal E3 cream 1.0 mg/g**
 - Insert ½ mL (0.5 mg E3) qhs x 21 nights, then 2-3x/week thereafter for maintenance
 - To help with vaginal dryness



E2 Patches



- Some are replaced TWICE weekly, while others are replaced ONCE weekly.
- Continuous E2 release.
- May lead to some dermatitis so pharmacists will often advise to “rotate” where the patches are applied to decrease the amount of time the patch is on a particular area of skin.

E2 Patch Dosing

Low

0.012 - 0.025 mg

High

0.1 mg

Most Common

0.05 mg

*Consider taking continuously or
as an on/off cycle and changed
1 - 2 times per week*



DUTCH BHRT Guide

DUTCH TESTING & (B)HRT GUIDE - WOMEN

Disclaimer: This form is a reference for providers and not to be considered medical advice or an endorsement of any particular HRT therapy. Any HRT may involve risks, and it is the sole responsibility of the provider to consider these risks and make treatment decisions.

Oral Progestrone	Estradiol Patch	Estradiol Cream/Gel	Testosterone or Estradiol Pellet	Vaginal Estrogen or Testosterone	Testosterone Cream/Gel	DHEA
Why						
Effective at balancing ERT, but clinical effects are due largely to metabolites formed in the gut. A good option when postmenopausal women struggle with sleep. A different ROA may be better for premenopausal women. 100-200mg has been shown to balance concurrent ERT.	Patches offer consistent hormone dosing over time and are very effective at managing hot flashes. Even low doses typically increase bone mineral density (BMD).	Proven to increase serum and urine levels as well as improve hot flashes and BMD. Transdermal E2 is attractive because it is easy to use and bypasses first pass metabolism. Estriol often given in doses 1 - 4 times higher than estradiol.	Pellets offer consistent hormone dosing over time for testosterone and estradiol. Research is limited on effects on hot flashes and BMD. Because serum/urine E2 levels match or exceed those seen in patches, E2 pellets are likely to help with hot flashes and BMD.	Low doses increase local tissue levels while higher doses also increase systemic levels. Placing in the top 1/3 of the vagina significantly increases uterine levels. Estriol often given in doses 1 - 4 times higher than estradiol.	Transdermal testosterone can be used to correct low T and improve sex drive and muscle mass.	Sublingual or oral DHEA will increase systemic levels and also contribute to downstream androgens (testosterone) and estrogens.
ERT, especially with an intact uterus, should be balanced with adequate progesterone (vaginal or oral preferred).						
Common Dosing Strategies						
Low 25 - 50 mg High >200 mg Most Common 100 - 200 mg <i>Consider taking continuously or as an on/off cycle</i>	Low 0.012 - 0.025 mg High 0.1 mg Most Common 0.05 mg <i>Consider taking continuously or as an on/off cycle and changed 1 - 2 times per week</i>	Low 0.1 - 0.25 mg Estradiol 0.1 - 1.0 mg Estriol High 1.0 - 2.5 mg Estradiol 2.0 - 5.0 mg Estriol Most Common 0.25 - 0.5 mg Estradiol 0.25 - 2.5 mg Estriol <i>Consider taking daily continuously or as an on/off cycle</i>	Low <5 mg Estradiol 20 - 50 mg Testosterone High >12 mg Estradiol >125 mg Testosterone Most Common 5 mg Estradiol 100 mg Testosterone <i>Inserted every 3 - 4 months</i>	Low 0.01 mg Estradiol 0.25 mg Testosterone High 0.5 mg Estradiol 2 mg Testosterone Most Common 0.1 mg Estradiol 0.25 - 1.0 mg Estriol 0.25 - 1.0 mg Testosterone <i>Taken daily, possibly with cycling</i>	Low 0.5 - 2.0 mg High 10 - 20 mg Most Common 1 - 5 mg <i>Taken daily, at waking or bedtime</i>	Low 1 - 5 mg High 25 - 50 mg Most Common 5 - 10 mg <i>Usually taken daily</i>
How to Monitor with DUTCH						
DUTCH results only show which metabolites are preferred. Evaluate which pathway is dominant (alpha or beta). If patients push down the alpha pathway, a lower dose may be used. Those who prefer beta metabolism and aren't sleeping well might benefit from a higher dose.	Monitoring Estrogen Replacement Therapy (ERT) Target values between the top of the postmenopausal range (0.7ng/mg for estradiol) and within the first third of the premenopausal range (about 2.5ng/mg). The specific target for a patient depends on the patient's history and symptoms as well as the patient and provider's comfort level with the risks for too much (breast cancer, etc.) and too little (osteoporosis, etc.) estrogen. It is recommended to closely monitor phase I metabolites to ensure that too many 4-OH metabolites are not formed. Methylation should also be evaluated and supported if inadequate. DUTCH OATs may also be helpful to ensure that a nutrient deficiency is not present. ERT may induce vitamin B6 deficiency. Proper metabolism requires B6, B12, and glutathione. For testosterone pellets, premenopausal levels should be targeted and patient symptoms monitored. Evaluate 5a-reductase activity before dosing with testosterone to ensure there isn't excessive 5a metabolism.			Levels above the postmenopausal range imply systemic uptake. For localized (vaginal) effects only, results should not exceed the postmenopausal range. Expect higher E2 levels compared to E1 and downstream metabolites. Progesterone metabolites underestimate systemic progesterone when taken vaginally.	It is optimal if levels of T (as well as metabolites) are in range. Less is needed if metabolites are 5a favored. Also monitor patient symptoms for excessive T. Transdermal progesterone, oral estrogen and sublingual hormones, are not well monitored by DUTCH and are not represented on this form along with a few other lesser used HRT options.	Monitor conversion to testosterone, E2 and metabolites of both. DHEA and testosterone metabolites may be artificially elevated if the patient doesn't skip the dose of DHEA the day of and day before the test (as described in the test instructions).



DUTCH BHRT Guide

Oral Progestrone	Estradiol Patch	Estradiol Cream/Gel	Testosterone or Estradiol Pellet	Vaginal Estrogen or Testosterone	Testosterone Cream/Gel	DHEA
Why						
Effective at balancing ERT, but clinical effects are due largely to metabolites formed in the gut. A good option when postmenopausal women struggle with sleep. A different ROA may be better for premenopausal women. 100-200mg has been shown to balance concurrent ERT.	Patches offer consistent hormone dosing over time and are very effective at managing hot flashes. Even low doses typically increase bone mineral density (BMD).	Proven to increase serum and urine levels as well as improve hot flashes and BMD. Transdermal E2 is attractive because it is easy to use and bypasses first pass metabolism. Estradiol often given in doses 1 - 4 times higher than estradiol.	Pellets offer consistent hormone dosing over time for testosterone and estradiol. Research is limited on effects on hot flashes and BMD. Because serum/urine E2 levels match or exceed those seen in patches, E2 pellets are likely to help with hot flashes and BMD.	Low doses increase local tissue levels while higher doses also increase systemic levels. Placing in the top 1/3 of the vagina significantly increases uterine levels. Estradiol often given in doses 1 - 4 times higher than estradiol.	Transdermal testosterone can be used to correct low T and improve sex drive and muscle mass.	Sublingual or oral DHEA will increase systemic levels and also contribute to downstream androgens (testosterone) and estrogens.
<i>ERT, especially with an intact uterus, should be balanced with adequate progesterone (vaginal or oral preferred).</i>						
Common Dosing Strategies						
Low 25 - 50 mg High >200 mg Most Common 100 - 200 mg <i>Consider taking continuously or as an on/off cycle</i>	Low 0.012 - 0.025 mg High 0.1 mg Most Common 0.05 mg <i>Consider taking continuously or as an on/off cycle and changed 1 - 2 times per week</i>	Low 0.1 - 0.25 mg Estradiol 0.1 - 1.0 mg Estradiol High 1.0 - 2.5 mg Estradiol 2.0 - 5.0 mg Estradiol Most Common 0.25 - 0.5 mg Estradiol 0.25 - 2.5 mg Estradiol <i>Consider taking daily continuously or as an on/off cycle</i>	Low <5 mg Estradiol 20 - 50 mg Testosterone High >12 mg Estradiol >125 mg Testosterone Most Common 5 mg Estradiol 100 mg Testosterone <i>Inserted every 3 - 4 months</i>	Low 0.01 mg Estradiol 0.25 mg Testosterone High 0.5 mg Estradiol 2 mg Testosterone Most Common 0.1 mg Estradiol 0.25 - 1.0 mg Estradiol 0.25 - 1.0 mg Testosterone <i>Taken daily, possibly with cycling</i>	Low 0.5 - 2.0 mg High 10 - 20 mg Most Common 1 - 5 mg <i>Taken daily, at waking or bedtime</i>	Low 1 - 5 mg High 25 - 50 mg Most Common 5 - 10 mg <i>Usually taken daily</i>

DUTCH BHRT Guide

Gels tend to absorb better than creams, but can be drying to the skin

Estradiol Cream/Gel	Vaginal Estrogen or Testosterone
Low 0.1 - 0.25 mg Estradiol 0.1 - 1.0 mg Estriol	Low 0.01 mg Estradiol 0.25 mg Testosterone
High 1.0 - 2.5 mg Estradiol 2.0 - 5.0 mg Estriol	High 0.5 mg Estradiol 2 mg Testosterone
Most Common 0.25 - 0.5 mg Estradiol 0.25 - 2.5 mg Estriol <i>Consider taking daily continuously or as an on/off cycle</i>	Most Common 0.1 mg Estradiol 0.25 - 1.0 mg Estriol 0.25 - 1.0 mg Testosterone <i>Taken daily, possibly with cycling</i>

Vaginal tissue is more efficient at absorbing hormones, so notice that we tend to use lower doses of E2 vaginally than we do topically!



Other Considerations:

- **Also remember to treat the gut, support the adrenals, regulate blood sugars, support the thyroid if indicated and support healthy estrogen metabolism pathways!**
- Cruciferous vegetables, carrot “apiaceae” family vegetables, rosemary and resveratrol can all help to “push” the “protective pathway” CYP1A1 enzyme towards the production of 2-OH metabolites. This may help to lower the 4-OH level.
- Sulforaphane and glutathione can protect the DNA from damage (if the 4-OH metabolites become reactive quinones) and can also support phase 2 detox (help clear 4-OH metabolites out of phase 1).



Recommended: Dr. Doreen Saltiel's Webinar on MHT



dutchtest.com/video/menopausal-hormone-therapy-clinical-benefits-and-outcome-studies



...and that concludes our webinar!

Thank you for listening.

Instagram



drkellyhead
Dr. Kelly Head, ND

Lecture questions?
info@dutchtest.com



Like Us, Follow Us, or Leave a Review!

<https://www.facebook.com/dutchtest>

<https://twitter.com/DutchTestLab>

<https://www.linkedin.com/company/10883377>

<https://www.instagram.com/dutchtest/>

<https://www.youtube.com/channel/UCauTDzKu4VS74PMiYgda-PQ>

