Understanding Fertility with the DUTCH Test

Dr. Jaclyn Smeaton, ND. Chief Medical Officer

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Reminder: Definition of Infertility

Absence of pregnancy or delivery of a live-born child after one year of unprotected intercourse

- Evaluation is warranted:
  - Any age with known or suspected barriers to pregnancy (family history, history of relevant medical concerns, etc)
  - After 1 year of timed intercourse for <35 years
  - After 6 months of timed intercourse for >=35 years

Standard Evaluation

- Documentation of ovulation
  - Patient history
  - Mid-luteal progesterone level >5 ng/mL
- Standard semen analysis
- HSG (Hysterosalpingogram), to test for tubal patency
- Assessment of ovarian reserve
  - Many options here (CD3 FSH, E2, AMH, Inhibin B)
- Diagnostic laparoscopy
  - When indicated by patient history, abnormal pelvic exam or abnormal HSG

the world underneath infertility

Evaluation for Patients with Infertility

Thorough intake

- Review of systems, health histories

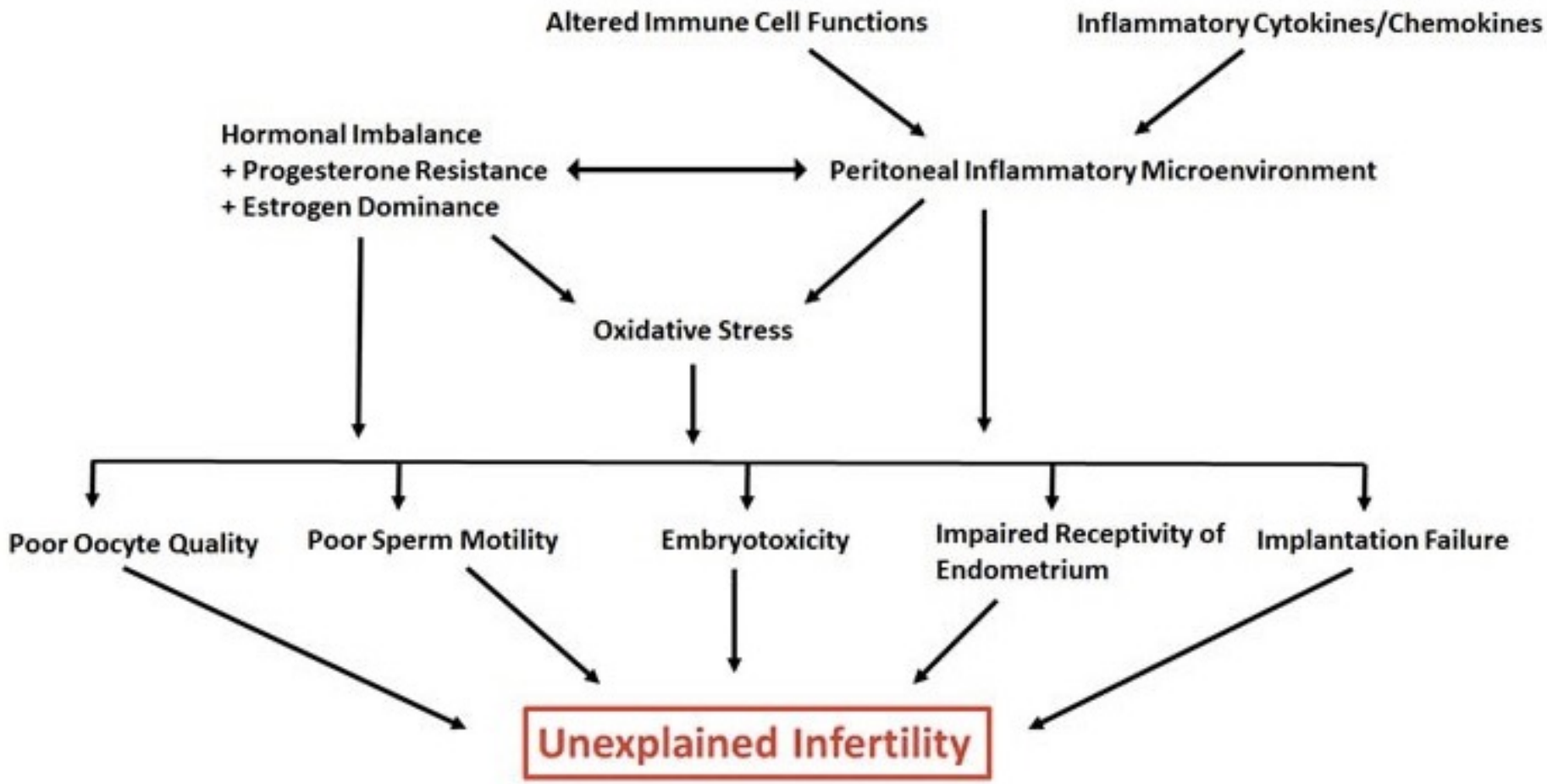
- Signs of underlying physiological patterns/problems?

  - Gut health (maldigestion, pain, gas/bloating, dysbiosis, abx use)
  - Infection (gut, chronic viral, etc)
  - Detoxification (liver, hormone detoxification & elimination)
  - Energy production (adrenal, thyroid, pancreas)
  - Oxidative imbalance (allergies, skin inflammation, itching, histamine issues, etc)
  - Immune balance/Inflammation: (frequent illness, AI in past/family hx, etc)
  - Hormonal imbalance (luteal phase defect, endometriosis)
  - Structural (endometriosis, fibroids, blocked tubes, etc)

Functional Medicine Model

Table 1. Assessments, Laboratory Findings and Treatments
Organized According to the Functional Medicine Matrix

Clinical Assessment	Initial Laboratory Results	Initial Recommended Treatment
Fundamental Lifestyle Factors: Nutrient Imbalances		
Hypertension Maldigestion/malabsorption (MSQ: GI)	Low B12 (elevated urinary methylmalonic acid) Low serum COQ10 Low serum vitamin D Low fecal elastase (poor digestion)	Methylcobalamin 5000ug SL QD CoQ10 300mg PO QD D3 5000IU PO QD HCL 500mg titrate to tolerance Digestive enzymes: 2 with main meals
Defense and Repair (e.g. Immune, Inflammation, Infection/microbiota)		
Food allergies/sensitivities Dysbiosis History of antibiotics Intestinal hyperpermeability (MSQ: GI, Joint, Energy) Environmental allergies (MSQ: Nose) Hypovitaminosis D	Celiac gene: HLADQ2 Low serum vitamin D IgG4 testing +3 to dairy, mild positives 5 additional foods Stool testing: microbiota imbalance, low fecal elastase (hs-CRP normal),	Vitamin D3, Digestive enzymes, HCL – as noted in "Nutrient Imbalances" Glutamine-based GI repair powder Probiotic combination:100 billion CFU per day **Dietary changes:** Lower carbohydrate, gluten and dairy-free, minimal sugar, protein at all meals. Whole foods, minimally processed, organic diet. Rotate mild reactants.
Assimilation (e.g. Digestion, Absorption, microbiota/GI, Respiration)		
Dysbiosis History of antibiotics Intestinal hyperpermeability Maldigestion/malabsorption (MSQ: GI)	Celiac gene: HLADQ2 (Celiac serology negative) IgG4 testing +3 to dairy, mild positives 5 additional foods Stool testing: microbiota imbalance	As noted in "Defense and Repair"
Communication (e.g. Endocrine, Neurotransmitters, immune messengers)		
Hypertension Hyperlipidemia Family history of heart disease and diabetes	Low HDL Low-normal free testosterone High-normal fasting blood glucose (thyroid panel, LDL, homocysteine, Lp(a), essential elements and amino acids all normal)	Dietary changes as noted in "Defense and Repair" Cardiovascular exercise prescription DHEA 50mg PO QD
Energy (e.g. Energy Regulation, Mitochondrial Function)		
MSQ: fatigue Statin rx	Low serum vitamin D Low serum CoQ10 B12 deficiency (cardiovascular, inflammatory and oxidative markers all within normal limits)	Alpha lipoic acid 200mg: 1 tab TID As noted in "Nutrient Imbalances"
Mental, Emotional, Spiritual		
High-stress work life	N/A	Pending retirement Exercise prescription



Oncotarget 2017 Jan 24;8(4):7138-47

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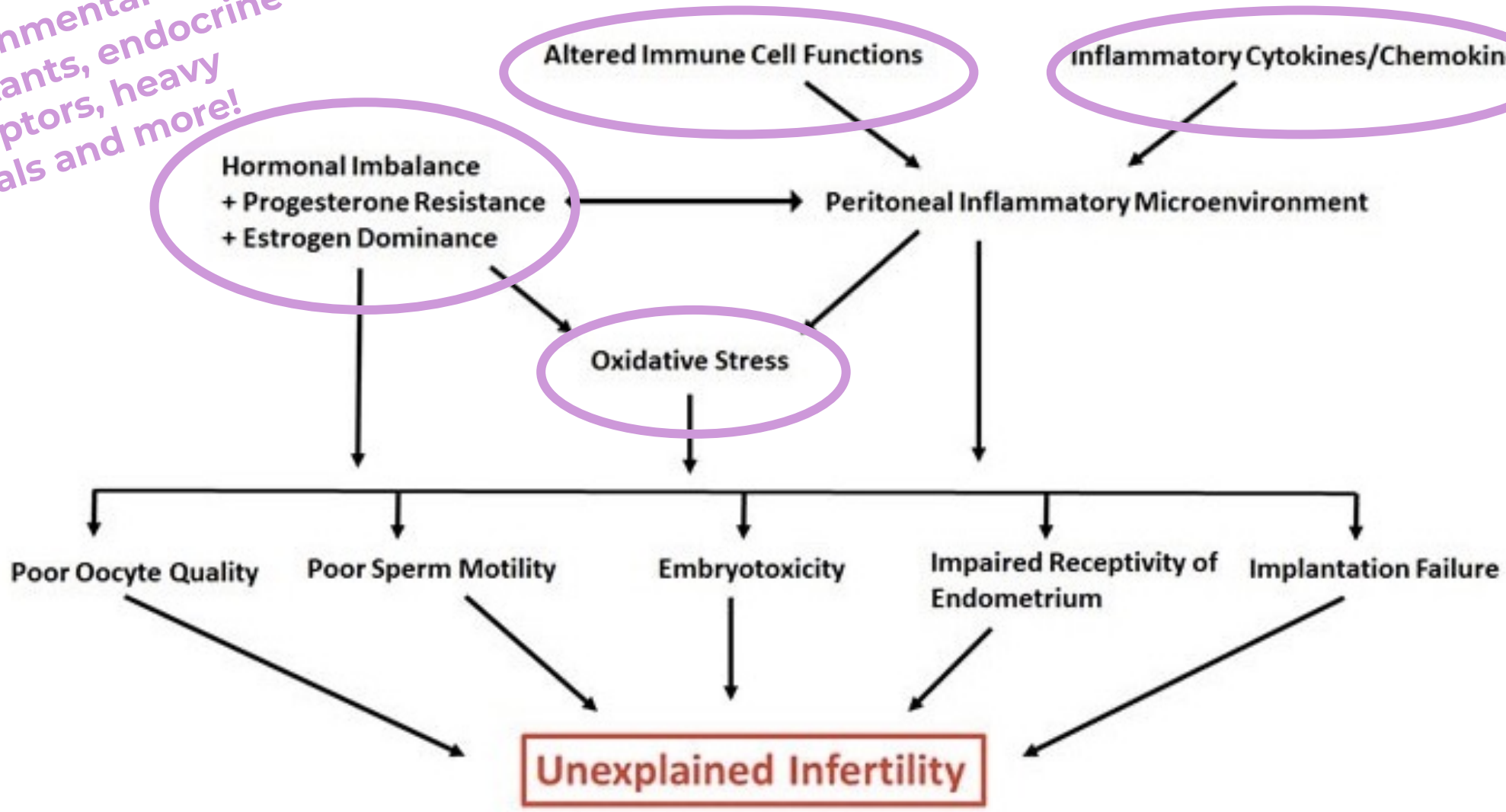
Environmental pollutants, endocrine disruptors, heavy metals and more!



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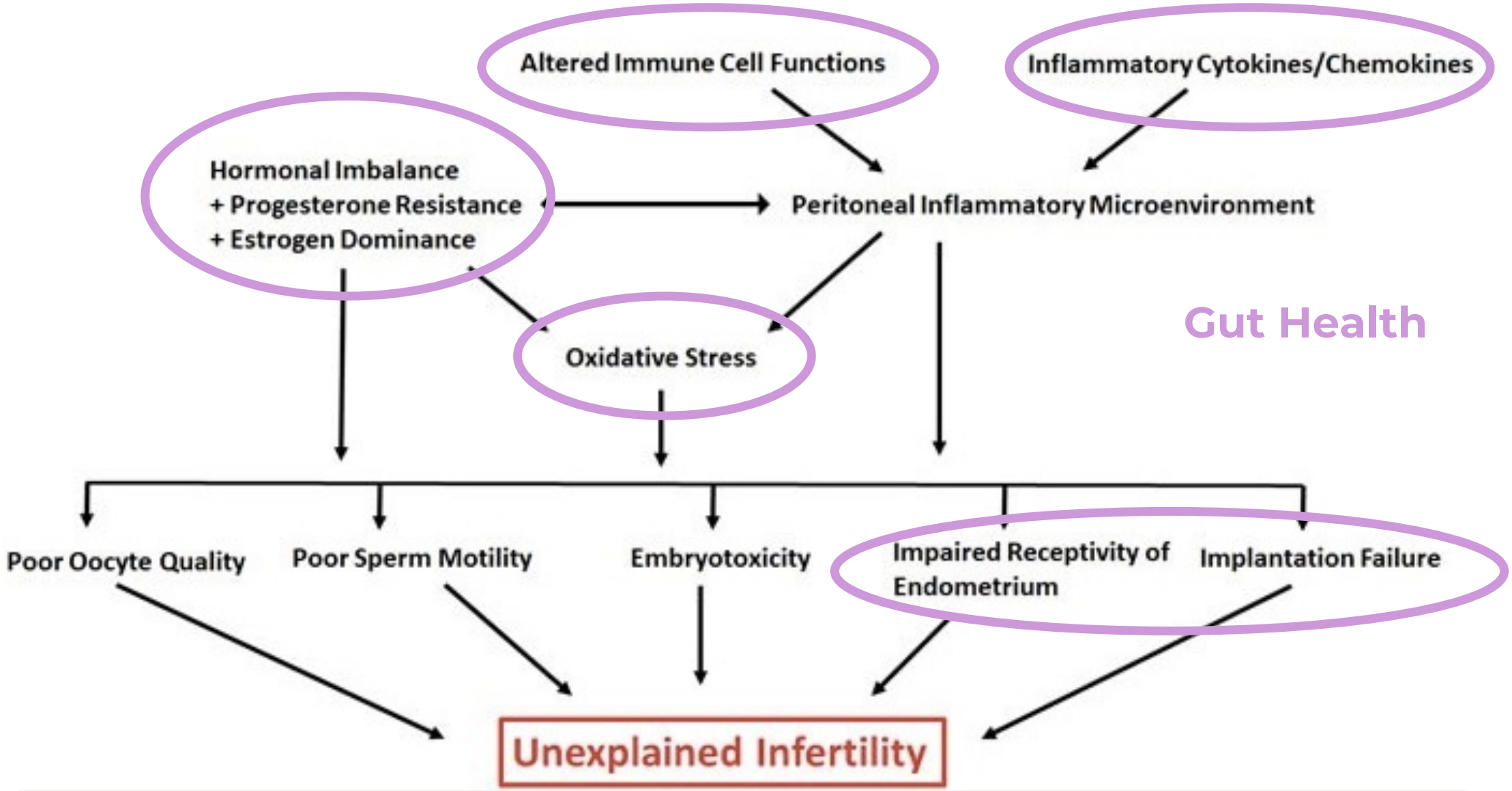

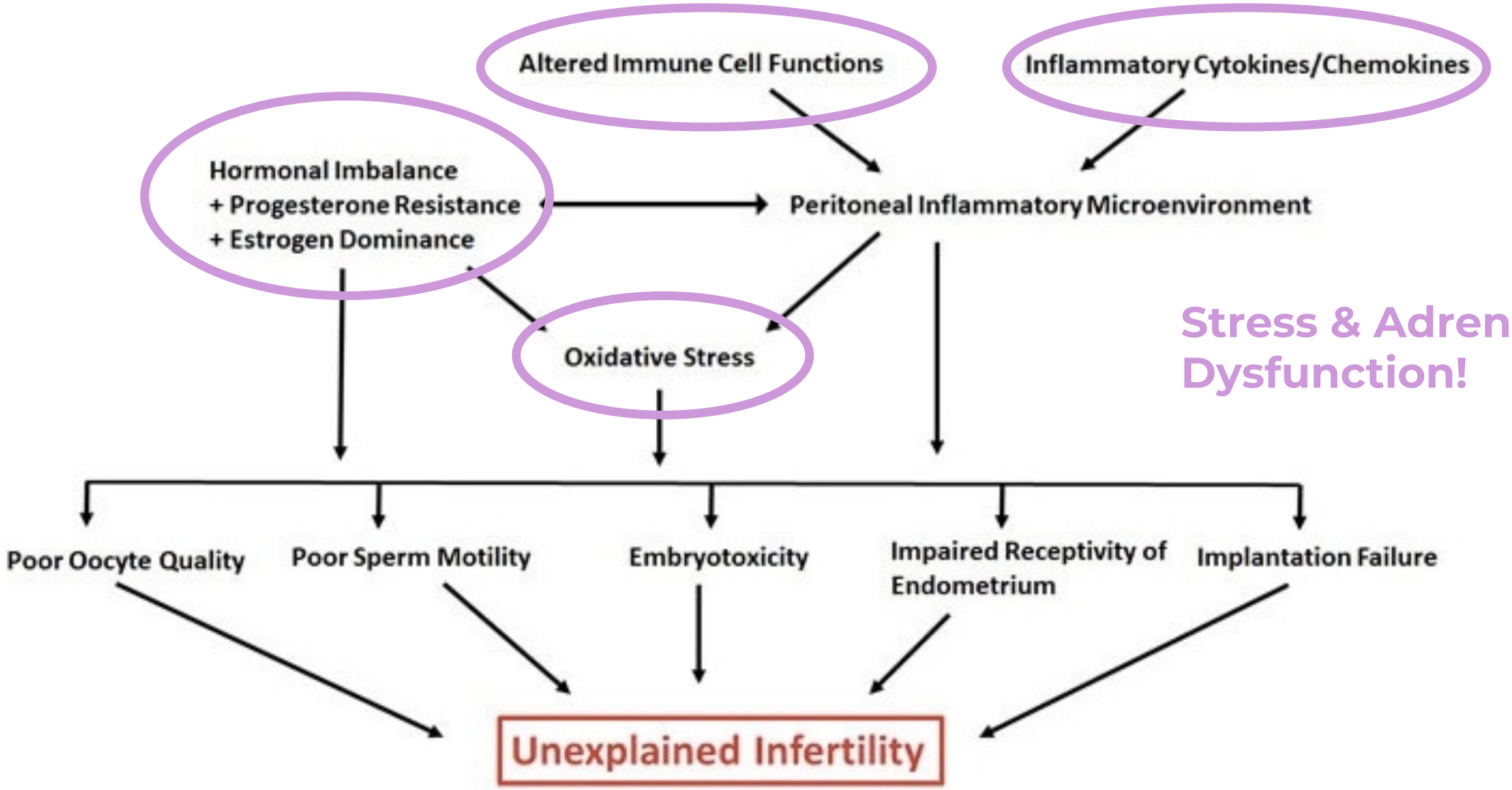

Stress & Adrenal Dysfunction!

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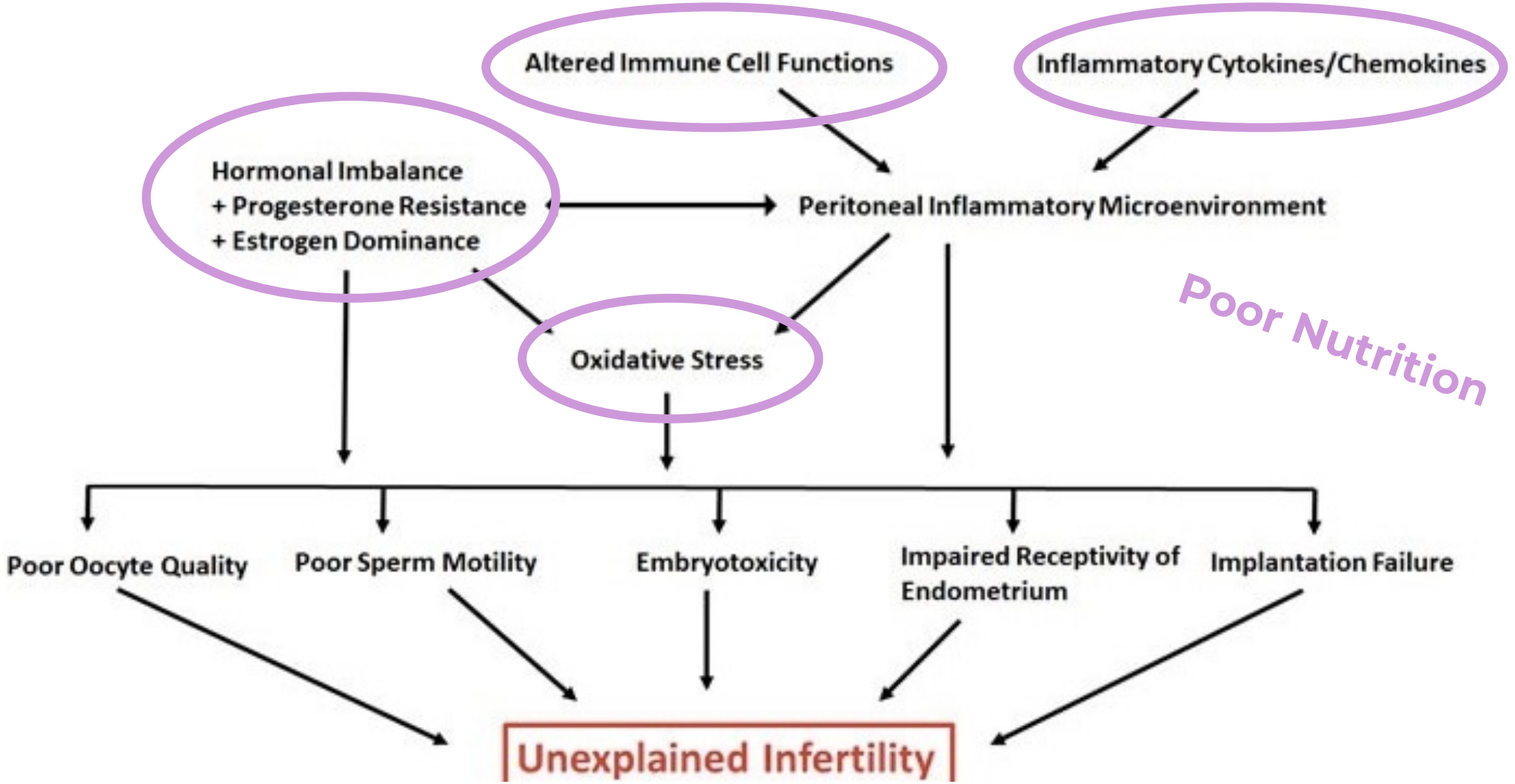
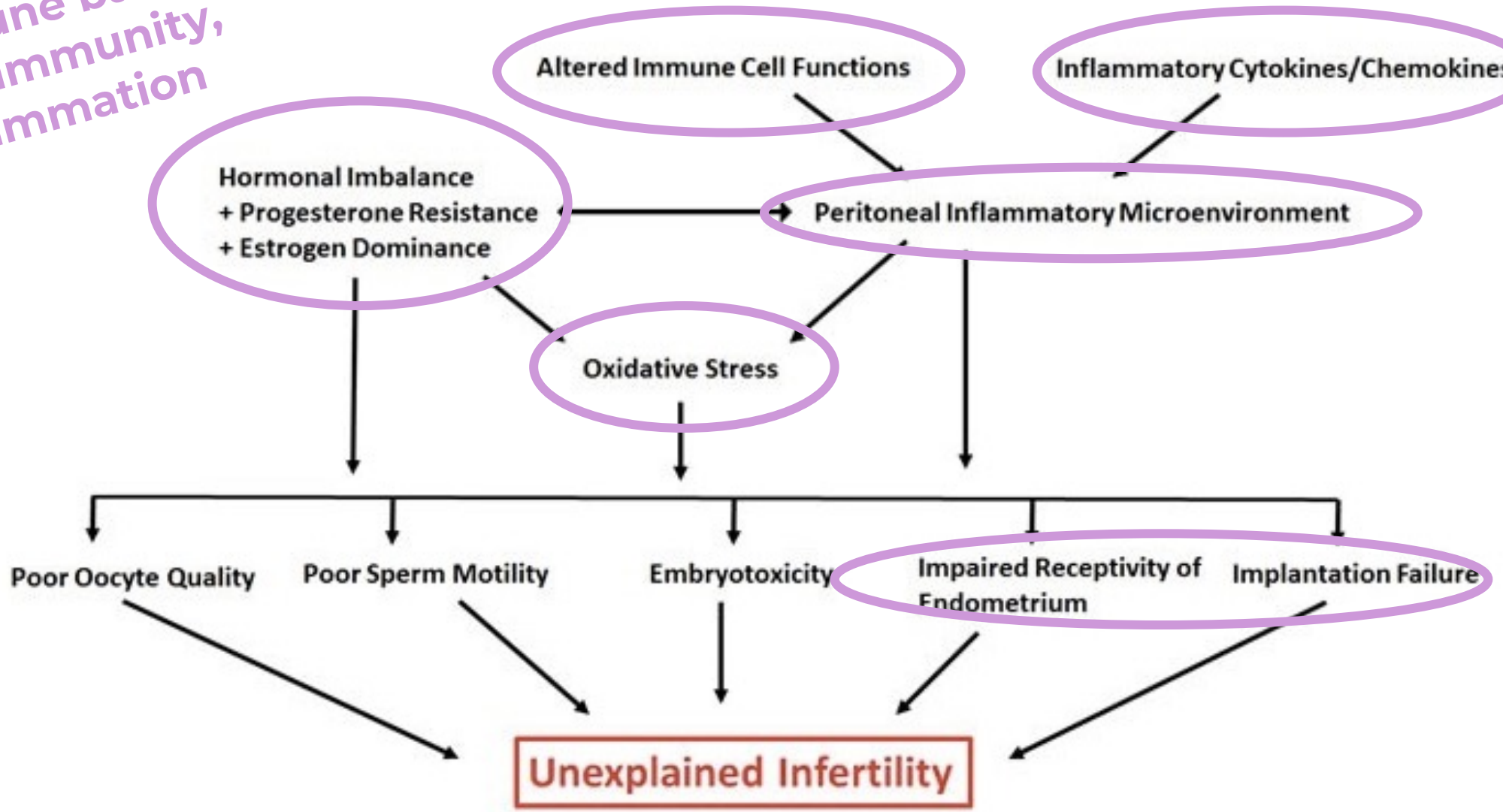


Immune balance, autoimmunity, inflammation



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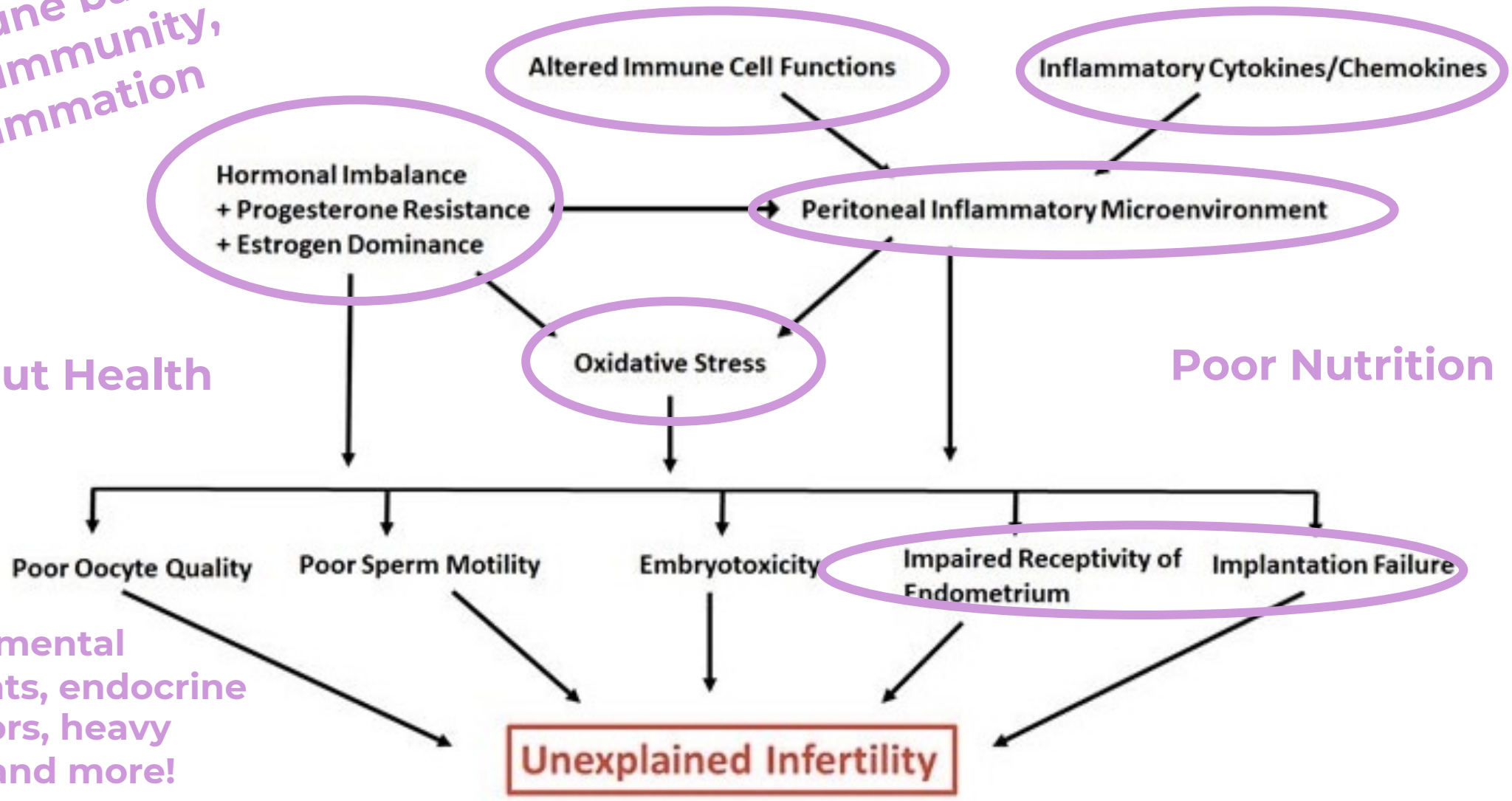
Immune balance, autoimmunity, inflammation

Stress & Adrenal Dysfunction!



Gut Health

Poor Nutrition

Environmental pollutants, endocrine disruptors, heavy metals and more!

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Physiological Area	Symptoms/Signs	Key DUTCH test analytes to review
Gut health	Abd pain, maldigestion, gas, bloating, irregular BMs, diarrhea, constipation, abx use, H pylori	Indican (gut dysbiosis marker) MMA, xanthurenate/kynurenate, b-Hydroxyisovalerate- (deficiency can be due to low stomach acid/poor absorption)
Infection	Fatigue, pain, cognitive, brain fog, history of exposure (travel, outdoor time, etc)	
Detoxification	Irregular BMs, fatigue, pain, brain fog	
Energy Production	Fatigue, muscle aches, anxiety, mood disorders, blood sugar imbalance	Organic Acids, fasting BG, fasting Insulin, A1c
Oxidative imbalance	Weight fluctuations, allergies, skin rashes, fatigue	Pyroglutamate (glutathione low) 8-OHdG, melatonin (key antiox)
Immune imbalance/inflammation	Frequent infection, pain, gut trouble, etc	See p140 - Quinolinate, (quinolinate/kynurenate ratio) hsCRP, sed rate, ANA, total IgA
Hormonal Imbalance	Menstrual irregularity, PMS, short luteal phase, scanty menses, heavy menses, endometriosis, OCP use, etc	DUTCH sex hormones, adrenal testing, complete thyroid
Structural	Suspected endometriosis, fibroids, blocked tubes, vaginal/reproductive dysbiosis	Ultrasound, laparoscopy, HSG, Mayan abdominal massage practitioner, Vaginosis profile

Hormonal Balance

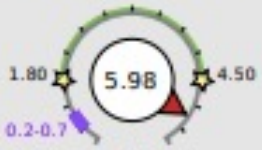
- Why is this important?
  - Proper cycle and adequate hormone levels to mature an egg, ovulate, and support implantation and pregnancy
- How can you assess with DUTCH?
  - Review sex hormones and metabolites
- Other labs that should be considered?
  - Great to also consider serum labs as previously mentioned

Hormone Testing Summary

Key (how to read the results):

Sex Hormones

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



Estradiol(E2)

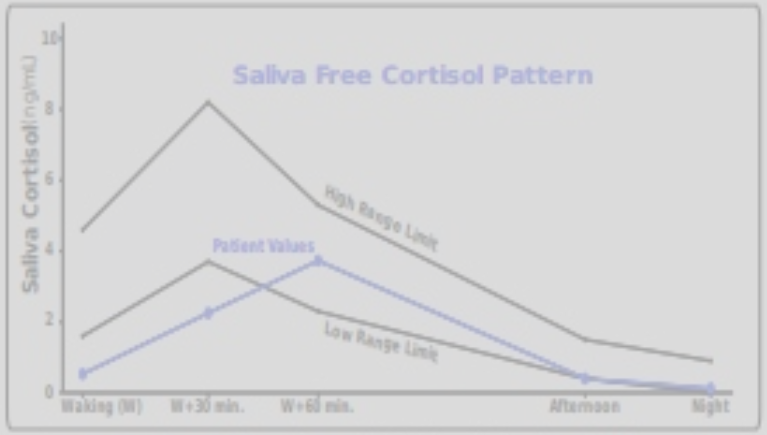
Progesterone
(Serum Equivalent, ng/mL)

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

Testosterone

Adrenal Hormones

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



Total DHEA Production

Age	Range
20-39	1300-3000
40-59	750-2000
>60	500-1200

Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)

Saliva Cortisol Total
(Sum of 5 values)

cortisol metabolism

Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

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

The following videos (which can also be found on the website under the listed names along with others) may aid your understanding:
DUTCH Plus Overview (quick overview) Estrogen Tutorial Female Androgen Tutorial Cortisol/CAR Tutorial

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

Estrogen

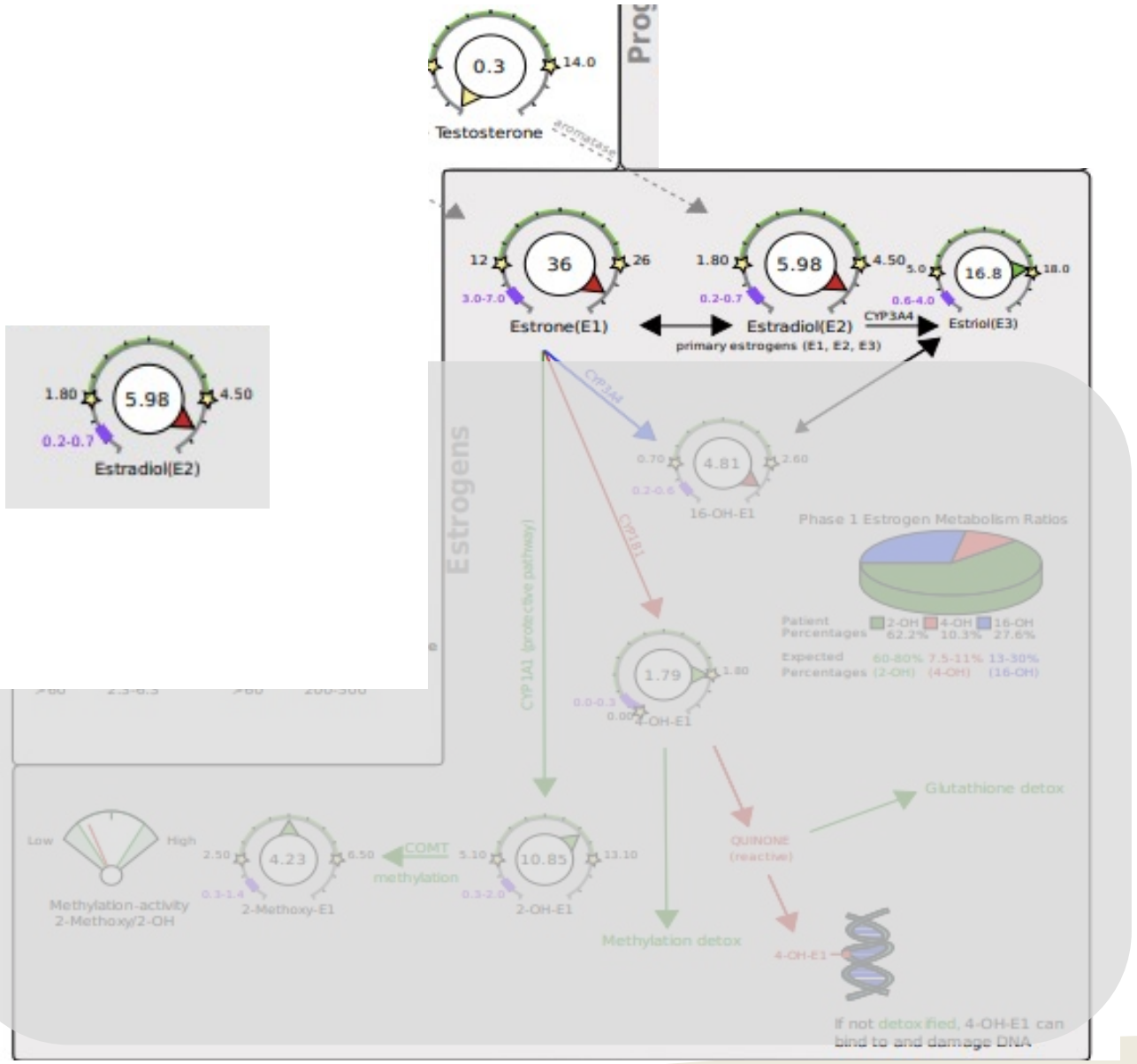
High

- Remember this is a luteal phase measurement
- Can be normal! Do they have signs/symptoms of high E?
    - Heavy bleeding, cramping, fibroids, tender breasts, etc
- Estrogen dominance picture due to exogenous exposures, high aromatase activity, poor detoxification, insulin resistance, obesity, inflammation, elevated androgens, gut dysbiosis, etc

Low

- Can be associated with: High stress (HPA axis dysfunction), thyroid dysfunction, high prolactin, low aromatase activity, low androgen levels, poor ovarian cell health & decreased ovarian blood flow, perimenopause
- Check for DIM use
- Often paired with symptoms like vaginal dryness, hot flashes, low sex drive, mood changes, and insomnia

Estrogen



Progesterone

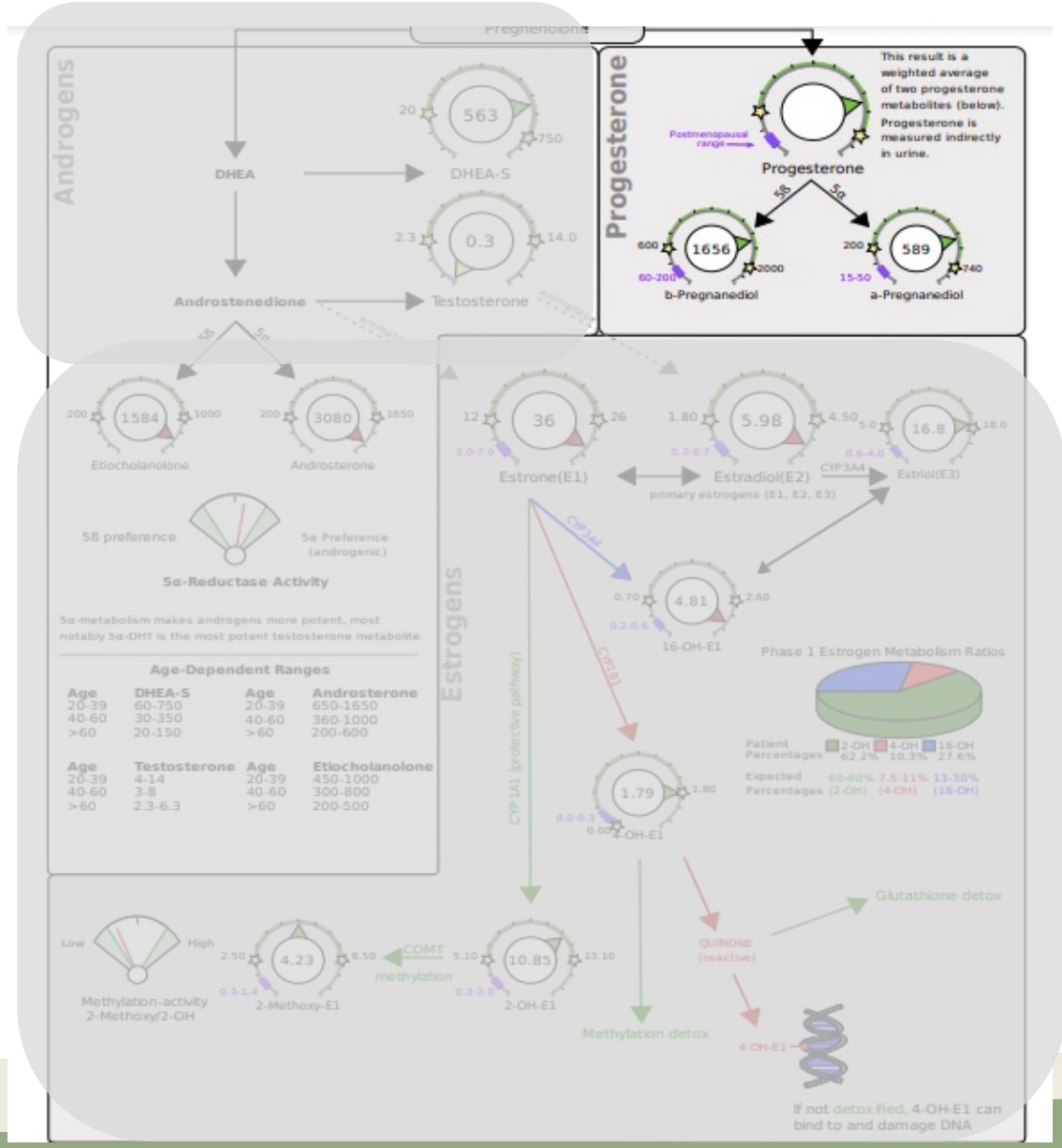
High

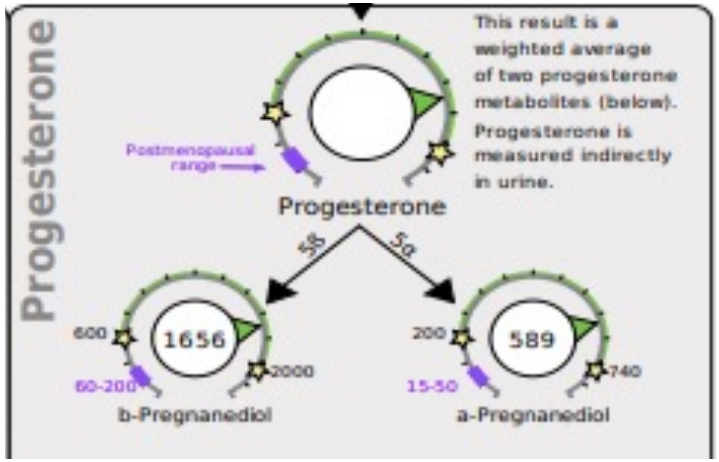
- Can be normal and asymptomatic!
- High progesterone can also be associated with supplementation, pregnancy, inflammation, HPA-axis dysfunction, obesity and insulin resistance.
- The ideal mid-luteal progesterone is above 15. Above 41 may result in lower pregnancy rates, according to research.

Low

- Can be associated with: Anovulation, stress, perimenopause, PCOS, thyroid disorders, high prolactin or medication use
    - OCPs, progestins, GnRH agonists, some fertility meds, glucocorticoids, NSAIDS
- Often paired with symptoms like fatigue, insomnia, irritability, anxiety, weight gain.
- If paired with E dominance, you might see. PMS, heavy bleeding and breast tenderness

Progesterone





Testosterone in Females

High

- High testosterone can be commonly associated with PCOS, low SHBG, low aromatase activity, stress, obesity and blood sugar dysregulation, inflammation, and DHEA or T supplementation
- Your patient might experience acne, oily skin, increased facial/body hair, thinning scalp hair, and mood changes (irritability and aggression, particularly)

Low

- Can be associated with: aging, elevated SHBG, low HPA output, poor ovarian production, diabetes, hypothyroidism, sleep disturbances, EDCs, zinc deficiency, and upregulated aromatase.
- Often paired with symptoms like fatigue, weight gain, mood changes, low libido, and trouble building muscle mass.

Testosterone in Males

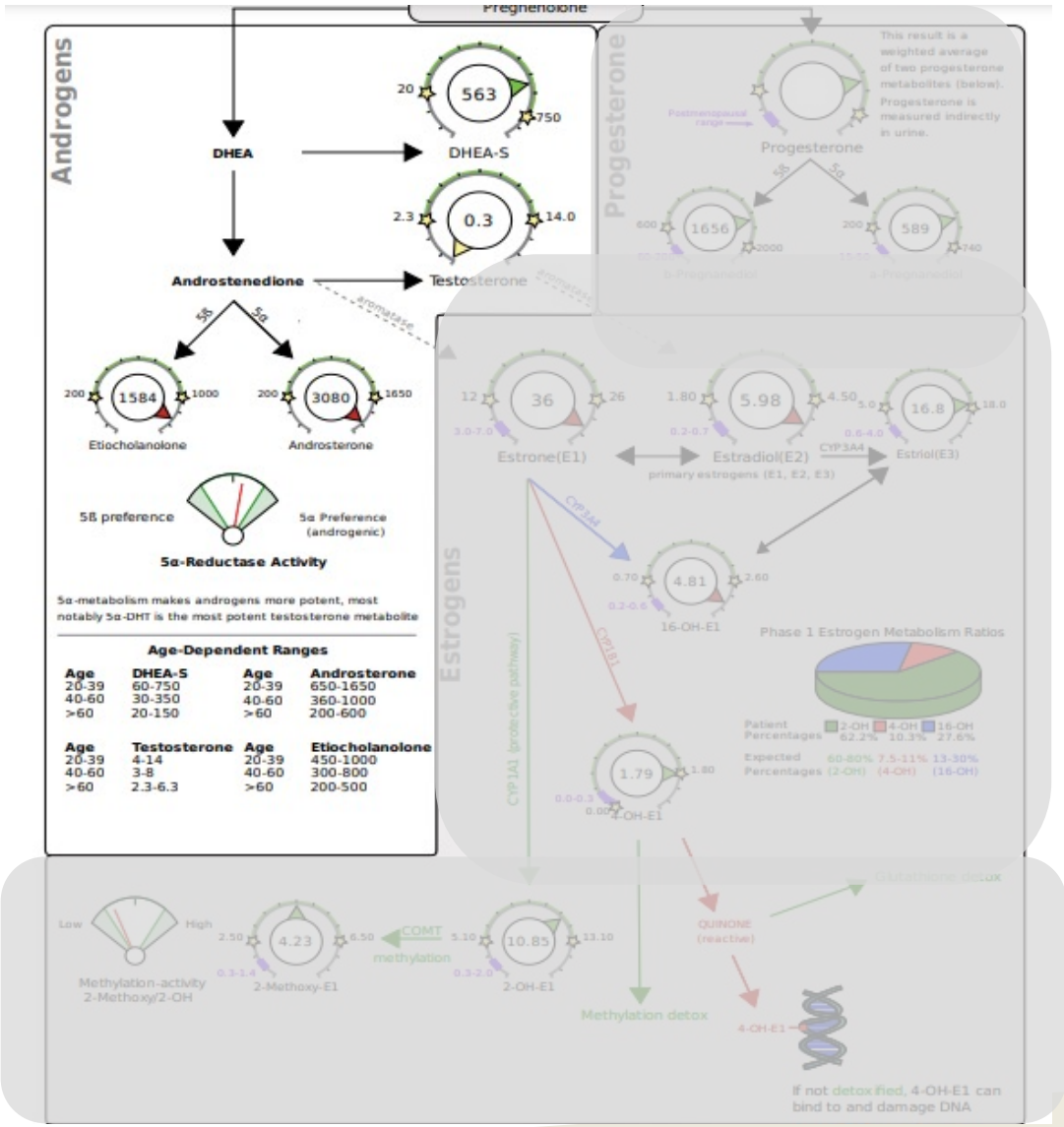
High

- High testosterone can be normal, or may be associated with low SHBG, downregulated aromatase activity, and certain medications and supplements.
- Important to note that TRT can cause low sperm production due to negative feedback
- Your patient might experience acne, oily skin, increased facial/body hair, thinning scalp hair, and mood changes (irritability and aggression, particularly)

Low

- Can be associated with: aging, elevated SHBG, low HPA output, poor ovarian production, diabetes, hypothyroidism, sleep disturbances, EDCs, zinc deficiency, regular THC use, and upregulated aromatase.
- Often paired with symptoms like fatigue, weight gain, mood changes, low libido, and trouble building muscle mass.

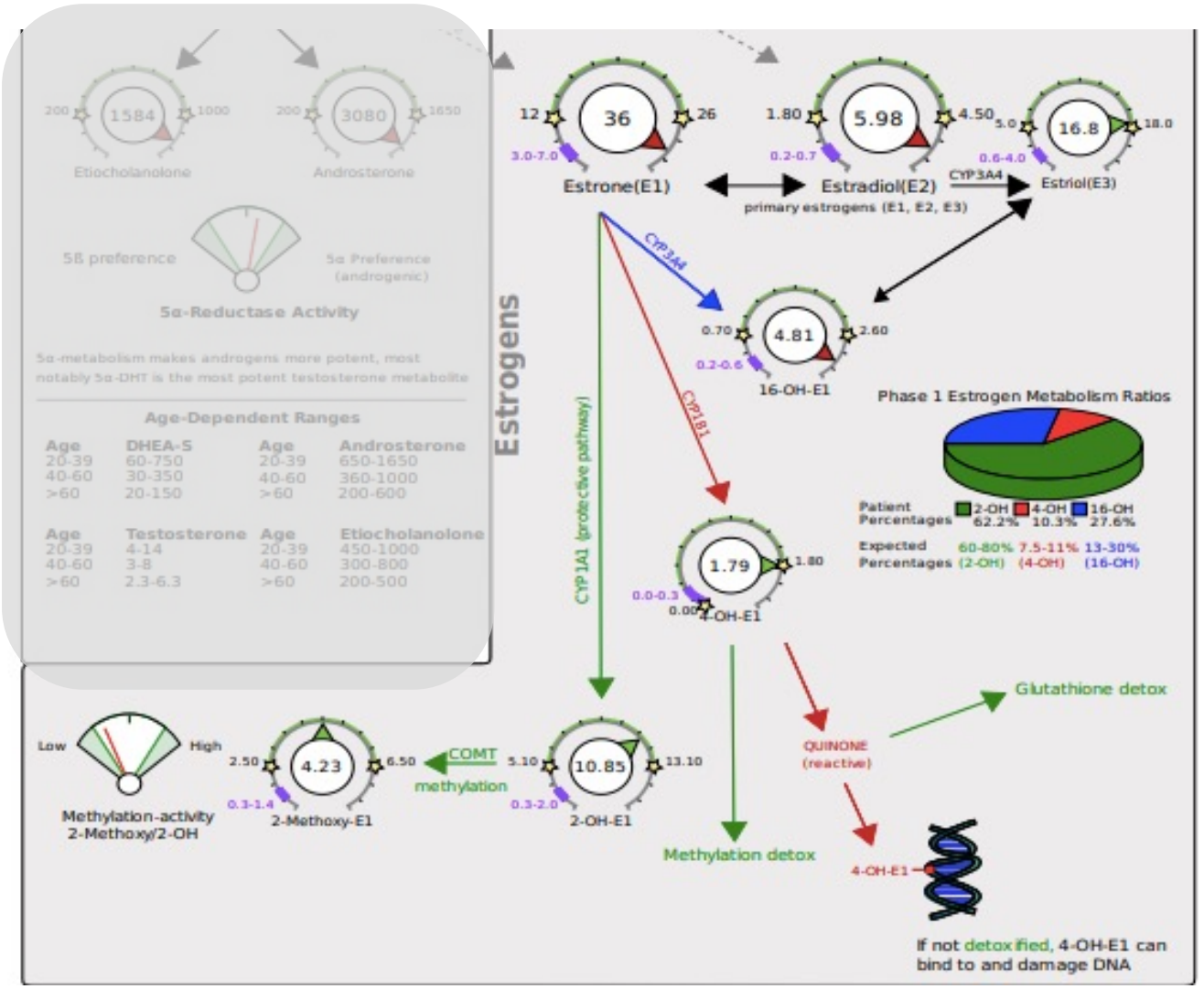
Testosterone



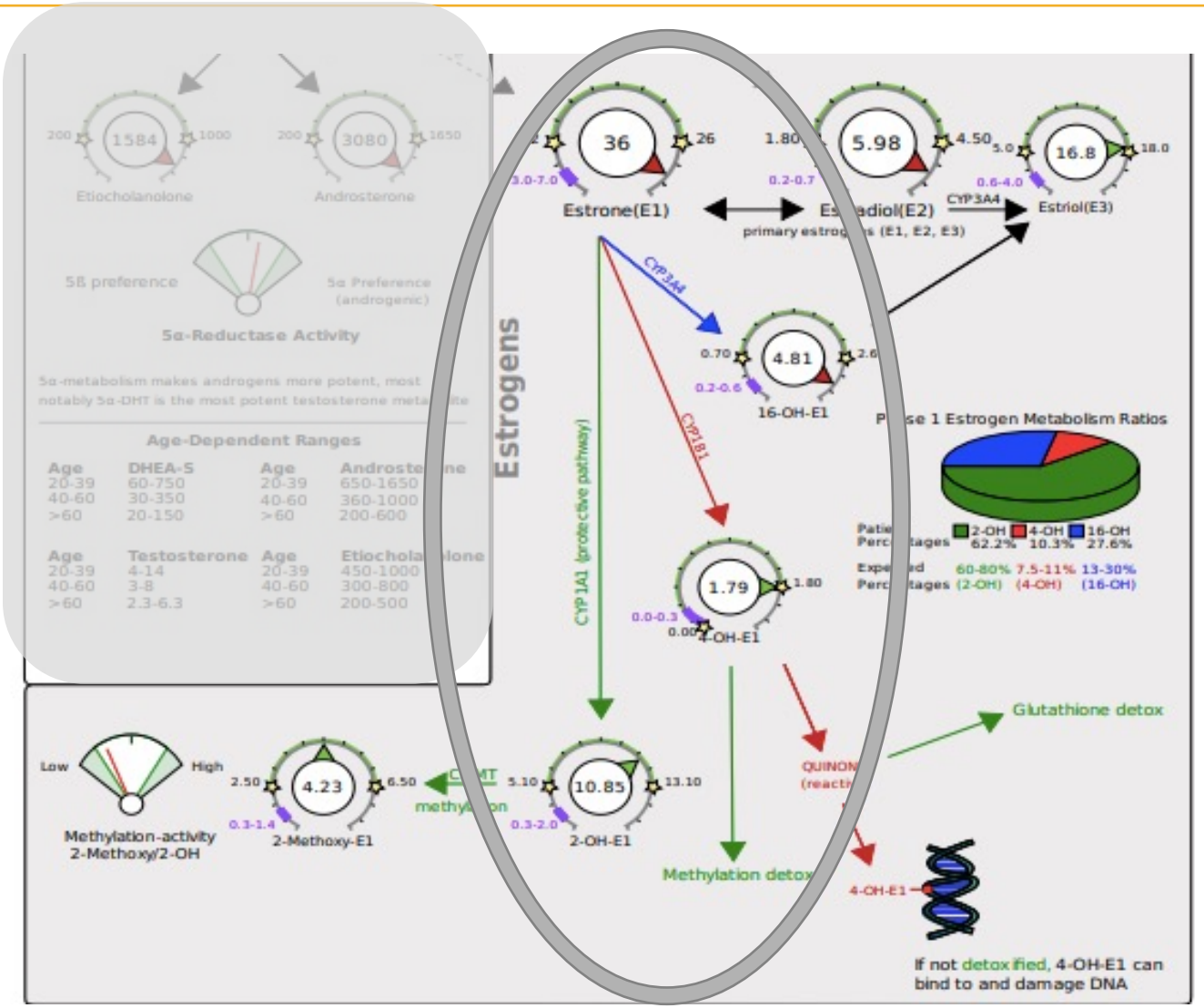
Estrogen Detoxification

Another critical aspect of hormonal health to review!

Estrogen Detoxification

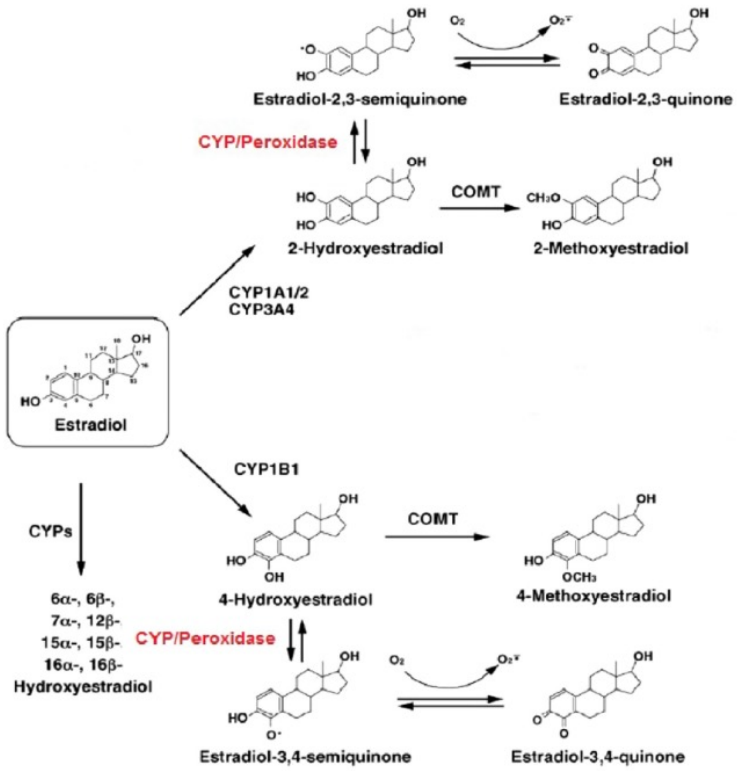


Estrogen Detoxification – Phase 1



Phase 1 Detoxification: Cytochrome Enzyme Systems

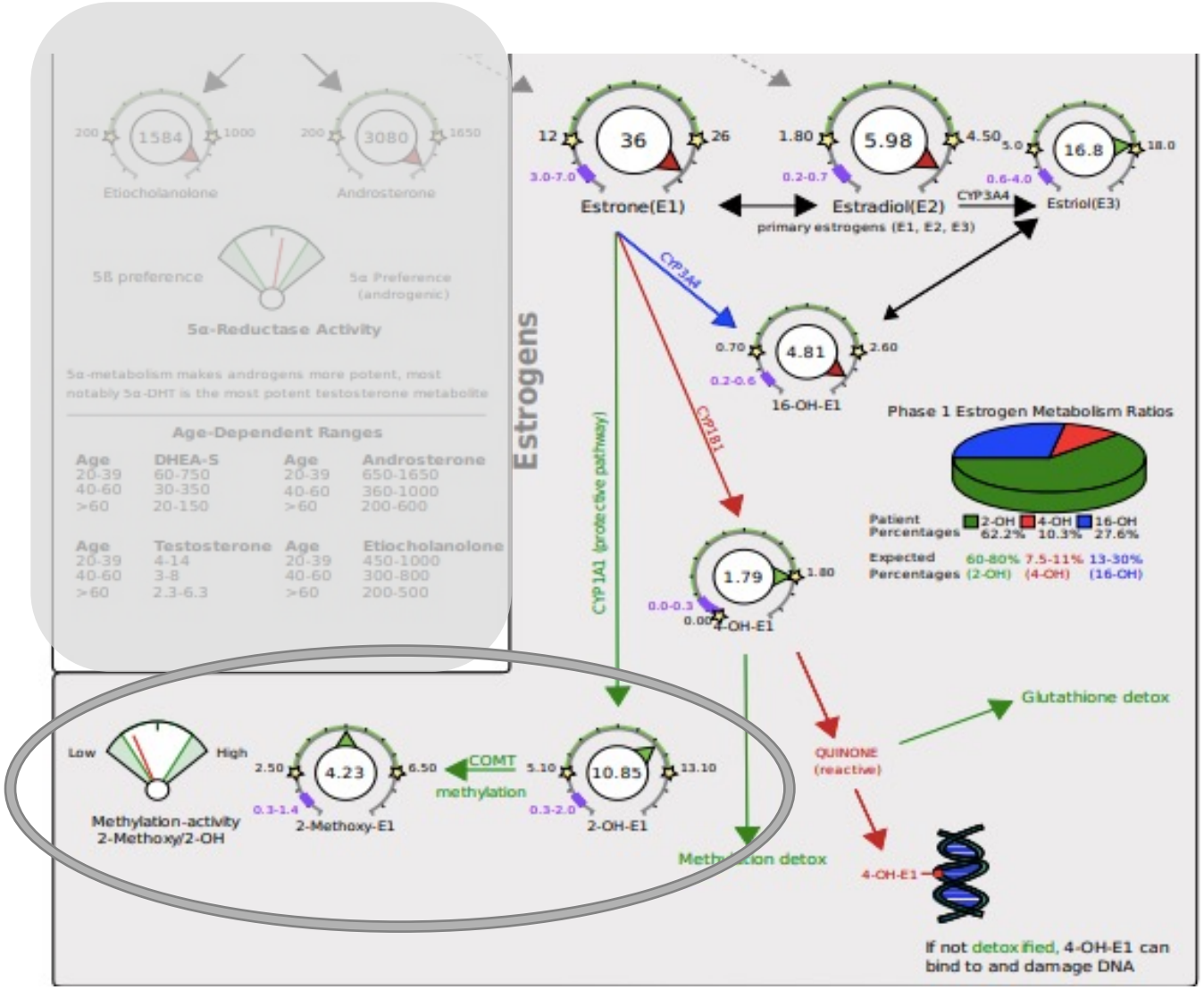
- Occurs mostly in the liver
- Estradiol is metabolized using CYP 1A1, 1A2, 1B1, and 3A4 enzymes, dependent on which is most available
- Estrogen undergoes the addition of a hydroxyl group (-OH)
- Highly reactive oxidative intermediates which need further transformation to be excreted
- Metabolites can still act on E receptors (weakly)
- Requires iron, good liver function, alcohol/meds can impede



Phase 1 Detoxification: Cytochrome Enzyme Systems

"2-OH" 2-hydroxyestrone & 2-hydroxyestradiol	"4-OH" 4-hydroxyestrone & 4-hydroxyestradiol	"16-OH" 16-hydroxyestrone
CYP1A1 & CYP1A2	CYP1B1	CYP3A4
Less carcinogenic and generally "preferred"	More carcinogenic	Proliferative Can be good for bones, but not so good with breast/fibroids/endo
Weakest binding potential to E receptor Anti-proliferative effects on cancer cell lines	If not properly metabolized, it can turn down a different pathway to become the free radical 3,4-quinone which can cause DNA damage	Binds most strongly to estrogen receptor, though still weakly
All of these metabolites are highly reactive oxidative intermediates- they require further biotransformation!		

Estrogen Detoxification – Phase 2



Phase 2 Detoxification: Methylation, Sulphation, Glucuronidation

- 2-OH & 4-OH catechol estrogens get a methyl group added by catechol-O-methyltransferase (COMT)
- Leads to production of
  - 2- and 4-methoxyestrone
  - 2- and 4-methoxyestradiol
- Conjugation with glucuronic acid and sulfate in liver more water soluble
- Sulphation & glucuronidation to support excretion thru bile into gut (like a package now, all tied up!)

Phase 3 Detoxification: Out of Cells & Into (& OUT OF!) Gut

- Estrogen metabolites leave the liver thru bile and are excreted through feces or urine
- B-glucuronidase
  - Found in tissues (ie breast) but also made in the gut by microbiome
  - When made in gut, estrogens can be recirculated rather than excreted, increasing estrogen load

Summary

	Phase 1: CYP Enzyme detox	Phase 2: Neutralization & water solubility	Phase 3: Excretion
Key steps	CYP enzymes convert estradiol into 3 main metabolites, 2-OH, 4-OH, 16-OH (which are oxidative!)	Neutrilazation of metabolites to avoid DNA damage and make more water soluble	Excretion out of liver cells and into bile to feces/urine (hopefully no excess B-glucuronidase and no excess reabsorption!)
Potential signs of a problem	Excess relative production of 4-OH or 16-OH metabolites	Poor methylation – see lower 2-Methoxy than 2-OH-E1 Anxiety (can also be linked to slow COMT)	BM infrequent Signs of estrogen dominance
How to help	Ensure liver function **Requires** Iron +DIM, I3C, quercetin, sulforaphane	+sulforaphane (if from food, requires stomach acid!) **Requires** SAMe, choline, Mg, TMG/betaine, methyl B12/folate/Bs, methionine, Zinc **INHIBITED BY:** E dominance, gut infxn, quercetin, green tea, PCBs, BPA, heavy metals, nutr deficiency	Improve the microbiome BM daily Ensure stomach acid Increase water, fiber + Prebiotics, Calcium D glucarate Unpeeled, raw carrots **AVOID:** antibiotics, junk food, alcohol

Oxidative Stress

- Why is this important?
  - Oxidative Stress is one of the key drivers for cell damage, and can affect eggs and sperm!

- How can you assess with DUTCH?
  - 8-OHdG (elevated)
  - Ptroglutamate (high or low) indicates low glutathione
  - Melatonin (low) – a critical antioxidant for fertility

Organic Acid Tests (OATs)

Ordering Provider:
Jaclyn Smeaton ND

DOB: 1985-03-12
Age: 36
Gender: Female

Last Menstrual Period:
2021-06-11

Collection Times:
2021-07-01 04:45AM (S)
2021-07-01 05:18AM (S)
2021-07-01 05:50AM (S)
2021-07-01 05:00PM (S)
2021-07-01 09:30PM (S)
2021-07-01 04:50AM (U)
2021-07-01 07:00AM (U)
2021-07-01 04:50PM (U)
2021-07-01 09:30PM (U)

Category	Test		Result	Units	Normal Range
Nutritional Organic Acids					
Vitamin B12 Marker (may be deficient if high) - (Urine)					
	Methylmalonate (MMA)	Within range	1.0	ug/mg	0 - 2.5
Vitamin B6 Markers (may be deficient if high) - (Urine)					
	Xanthurenate	Within range	0.20	ug/mg	0.12 - 1.2
	Kynurenate	Within range	1.4	ug/mg	0.8 - 4.5
Glutathione Marker (may be deficient if low or high) - (Urine)					
	Pyroglutamate	Within range	47.5	ug/mg	28 - 58
Neurotransmitter Metabolites					
Dopamine Metabolite - (Urine)					
	Homovanillate (HVA)	Low end of range	4.1	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite - (Urine)					
	Vanilmandelate (VMA)	Within range	2.9	ug/mg	2.2 - 5.5
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)					
	Melatonin* (Waking)	Above range	822.2	ng/mg	10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)					
	8-OHdG (Waking)	Within range	2.2	ng/mg	0 - 5.2

Physiological Area	Symptoms/Signs	Key DUTCH test analytes to review
Gut health	Abd pain, maldigestion, gas, bloating, irregular BMs, diarrhea, constipation, abx use, H pylori	Indican (gut dysbiosis marker) MMA, xanthurenate/kynurenate, b-Hydroxyisovalerate- (deficiency can be due to low stomach acid/poor absorption)
Infection	Fatigue, pain, cognitive, brain fog, history of exposure (travel, outdoor time, etc)	
Detoxification	Irregular BMs, fatigue, pain, brain fog	
Energy Production	Fatigue, muscle aches, anxiety, mood disorders, blood sugar imbalance	Organic Acids, fasting BG, fasting Insulin, A1c
Oxidative imbalance	Weight fluctuations, allergies, skin rashes, fatigue	Pyroglutamate (glutathione low) 8-OHdG, melatonin (key antiox)
Immune imbalance/inflammation	Frequent infection, pain, gut trouble, etc	See p140 - Quinolinate, (quinolinate/kynurenate ratio) hsCRP, sed rate, ANA, total IgA
Hormonal Imbalance	Menstrual irregularity, PMS, short luteal phase, scanty menses, heavy menses, endometriosis, OCP use, etc	DUTCH sex hormones, adrenal testing, complete thyroid
Structural	Suspected endometriosis, fibroids, blocked tubes, vaginal/reproductive dysbiosis	Ultrasound, laparoscopy, HSG, Mayan abdominal massage practitioner, Vaginosis profile

Inflammation and Immune Imbalance

- Why is this important?
  - Immune balance is critical for fertility
  - Affects hormone levels, detoxification, immune reaction (think implantation) and so much more!
- How can you assess with DUTCH?
  - Covered on the next page
- Other labs that should be considered?
  - hsCRP, sed rate, ANA, total IgA

Common Patterns with Inflammation on DUTCH

- 5a-reductase upregulated
- Aromatase upregulated (testosterone's to E2 and androstenedione to E1 conversion)
- DHEA-S lower compared to metabolites etiocholanolone and androsterone
- Estrogen clearance favoring 4-OH and/or 16-OH
- Elevated cortisol metabolism rate
- Elevated free cortisol
- Cortisol metabolism favoring THE (with chronic inflammation)
- Elevated Kynurenate, Quinolinate, and 8-OHdG
- Low or elevated pyroglutamate
- Elevated indican (if GI is involved)

Toxic Exposures & Detoxification

- Why is this important?
  - Toxic exposures can impact fertility in a number of ways, including affecting cell health (sperm and egg) as well as inflammation, hormone levels, and more!
- How can you assess with DUTCH?
  - Look for signs of inflammation and oxidative stress
  - Hormone imbalances, usually leaning towards estrogen dominance pattern
- Other labs that should be considered?
  - Consider full toxin panel testing if warranted

Screening for Toxin Risk with Pizzorno's Toxin

Screening tool

(adapted from The Toxin Solution by Joe Pizzorno, ND)

Test Name	Typical toxins affecting	"Normal Range"	Toxic range	Toxic Score	Your level	Your toxic score
ALT (alanine aminotransferase)	Cadmium, lead, mercury, OCPs, PCBs	0-35 U/L	0-24	0		
			25-30	1		
			31-35	2		
AST (Aspartate aminotransferase)	OCPs	0-35 U/L	0-23	0		
			24-26	1		
			27-35	2		
Bilirubin (total)	PCBs, PFOAs, PFQs	0.3-1.2 mg/dL	0.3-0.7	0		
			0.8-1.0	1		
			1.1-1.2	2		
LDL-cholesterol	PCBs	<130 mg/dL	<110	0		
			110-130	1		
GGTP (gamma-glutamyltransferase)	Most toxins	10-50 U/L	10-20	0		
			21-30	2		
			31-45	4		
			46-50	8		
HbA1C	Most POPs	4.0-8.5%	4.0-5.5	0		
			5-6-6.0	1		
			6.1-6.4	3		
			>6.4	5		
Homocysteine	Cadmium, lead	4-12 umol/L	4.0-8.0	0		
			8.1-10.0	1		
			10.1-12	2		
Platelet Count	Benzene, solvents	150-400	150-200	2		
			201-250	1		
			251-400	0		
T3 total	PCBs, PFOAs	0.7-1.5 ng/dL	0.7-0.8	2		
			0.9-1.0	1		
			1.1-1.5	0		
T4 total	PCBs	4.9-11.7 ng/dL	4.9-5.9	2		
			6.0-7.9	1		
			8.0-11.7	0		
Uric Acid (blood)	PFOAs, PFOS	2.5-8.0 mg/dL	2.5-5.3	0		
			5.4-5.6	1		
			5.7-5.8	3		
			>5.8	5		
WBC Count (white blood cell)	Benzene, CD, OCPs, PCBs	4,000-10,000	4000-5000	3		
			5,001-6,000	2		
			6,001-7,000	1		
			7,001-10,000	0		
TOTAL SCORE						

Interpreting your results

Low toxin load: <5.0
Marginally toxic: 5.1-10.0
Modestly toxic: 10.1- 15.0
Highly toxic: >15.0

Or the IFM

Toxin Exposure

Questionnaire

THE INSTITUTE FOR FUNCTIONAL MEDICINE®

Toxin Exposure Questionnaire

Patient Name_____ Date_____

Please check the best response for each of the following questions. Your provider will discuss your answers with you.

FOOD & WATER	YES	SOMETIMES	IN THE PAST	NO
1. Do you consume conventionally-farmed (non-organic) or genetically-modified fruits and vegetables?	☐	☐	☐	☐
2. Do you consume conventionally-raised (non-organic) animal products (i.e., meat, poultry, dairy, eggs)	☐	☐	☐	☐
3. Do you consume canned or farmed fish and seafood?	☐	☐	☐	☐
4. Do you consume processed foods (i.e., foods with added artificial colors, flavors, preservatives, or sweeteners), deep-fried, or fast foods?	☐	☐	☐	☐
5. Do you drink water from a well, spring, or cistern, or from plumbing pipes or fixtures installed before 1986?	☐	☐	☐	☐
6. Do you drink sodas, juices, or other beverages with natural or refined sweeteners (i.e., high-fructose corn syrup, cane sugar, agave nectar, Stevia, undiluted fruit juice, etc.) or artificial sweeteners (i.e., NutraSweet/Equal/aspartame, Sweet'N Low/saccharine, Splenda/sucralose, Sunett/Sweet One/acesulfame K, neotame)?	☐	☐	☐	☐

HOME & WORK ENVIRONMENT	YES	SOMETIMES	IN THE PAST	NO
1. Do you live in an apartment or home built before 1978, or in a mobile home, boat, or RV?	☐	☐	☐	☐
2. Does your home or workplace contain new construction materials or furniture (i.e., paint, laminate flooring, particle board, new carpeting, bedding, furniture, etc.)?	☐	☐	☐	☐
3. Does your home or workplace show signs of mold or water damage (i.e., cracking paint, ceiling leaks, decaying insulation or foam, visible mold, or damp windows, basement, or crawlspaces, etc.)?	☐	☐	☐	☐
4. Are you exposed to toxic substances (i.e., treated lumber, lead paint, paint chips or dust, broken mercury thermometers or fluorescent bulbs, etc.) at home or work?	☐	☐	☐	☐
5. Are you exposed to conventional cleaning chemicals, disinfectants, hand sanitizers, air fresheners, scented candles, or other scented products at home or work?	☐	☐	☐	☐
6. Do you live or work near an industrial pollution source (i.e., highway, factory, incinerator, gas station, power plant, etc.)?	☐	☐	☐	☐
7. Do you live or work near a source of electromagnetic radiation (i.e., cell phone tower, high-voltage power lines, or other known source)?	☐	☐	☐	☐
8. Do you live or work in an agricultural area or another type of area where you are exposed to herbicides, pesticides, or fungicides?	☐	☐	☐	☐
9. Do you have wood-burning, propane, or gas stoves or appliances at home or work?	☐	☐	☐	☐
10. Do you live or work in a sealed building with recirculated air?	☐	☐	☐	☐

Version 3

dutch®

Common Patterns with Suboptimal Sulfation on DUTCH

- Sulfation is critical for detoxification of estrogen and other compounds, free radicals, and ROS. Methionine and cysteine (S-containing AAs) are required for SAMe & glutathione production also!
  - Low DHEA-S relative to total DHEA
  - Elevated 16-OH-E1 relative to 4-OH and 2-OH
  - Elevated E3 relative to E1 and E2
  - Low melatonin

Mitochondrial Health and Energy Production

- Why is this important?
  - Mitochondria are critically important for healthy cells, including egg and sperm!
  - Early embryonic development is also very energy intensive
- How can you assess with DUTCH?
  - 8-OHdG (high)
  - Pyroglutamate (high or low)
  - Mitochondrial function and oxidative stress go hand in hand!
- Other labs that should be considered?
  - Consider nutrient testing for CoQ10 and other mito-necessary nutrients

Gut Health

- Why is this important?
  - GI function can:
    - Contribute to inflammation & oxidative stress
    - Affect hormone levels
    - Affect microbiome health
- How can you assess with DUTCH?
  - Indican (high)
  - Indirectly, through estrogen levels
- Other labs that should be considered?
  - Consider broader GI panel or microbiome assessment if warranted

Other Considerations

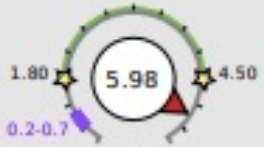
- Microbiome
  - GI, oral, and reproductive microbiomes
  - Finding a good partner for comprehensive analysis of microbiomes
- Structural Evaluations
  - Looking at endometriosis, fibroids, blocked fallopian tubes, etc.
  - May require additional workup such as ultrasound, HSG, laparoscopy, etc.

Hormone Testing Summary

Key (how to read the results):

Sex Hormones

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



Estradiol(E2)

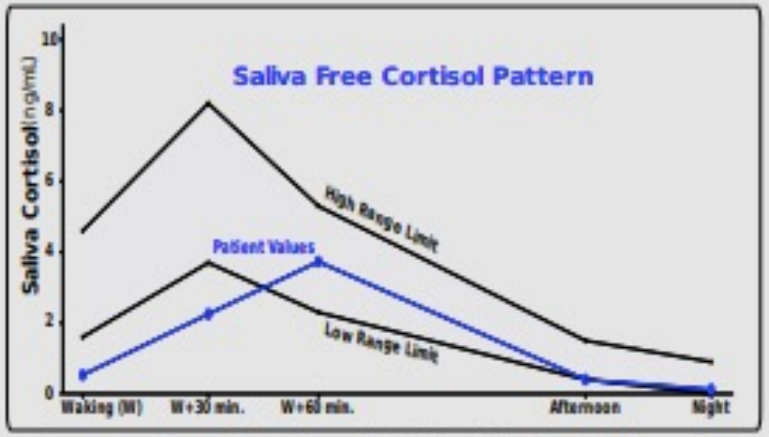
Progesterone
(Serum Equivalent, ng/mL)

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

Testosterone

Adrenal Hormones

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



Total DHEA Production

Age	Range
20-39	1300-3000
40-59	750-2000
>60	500-1200

Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)

Saliva Cortisol Total
(Sum of 5 values)

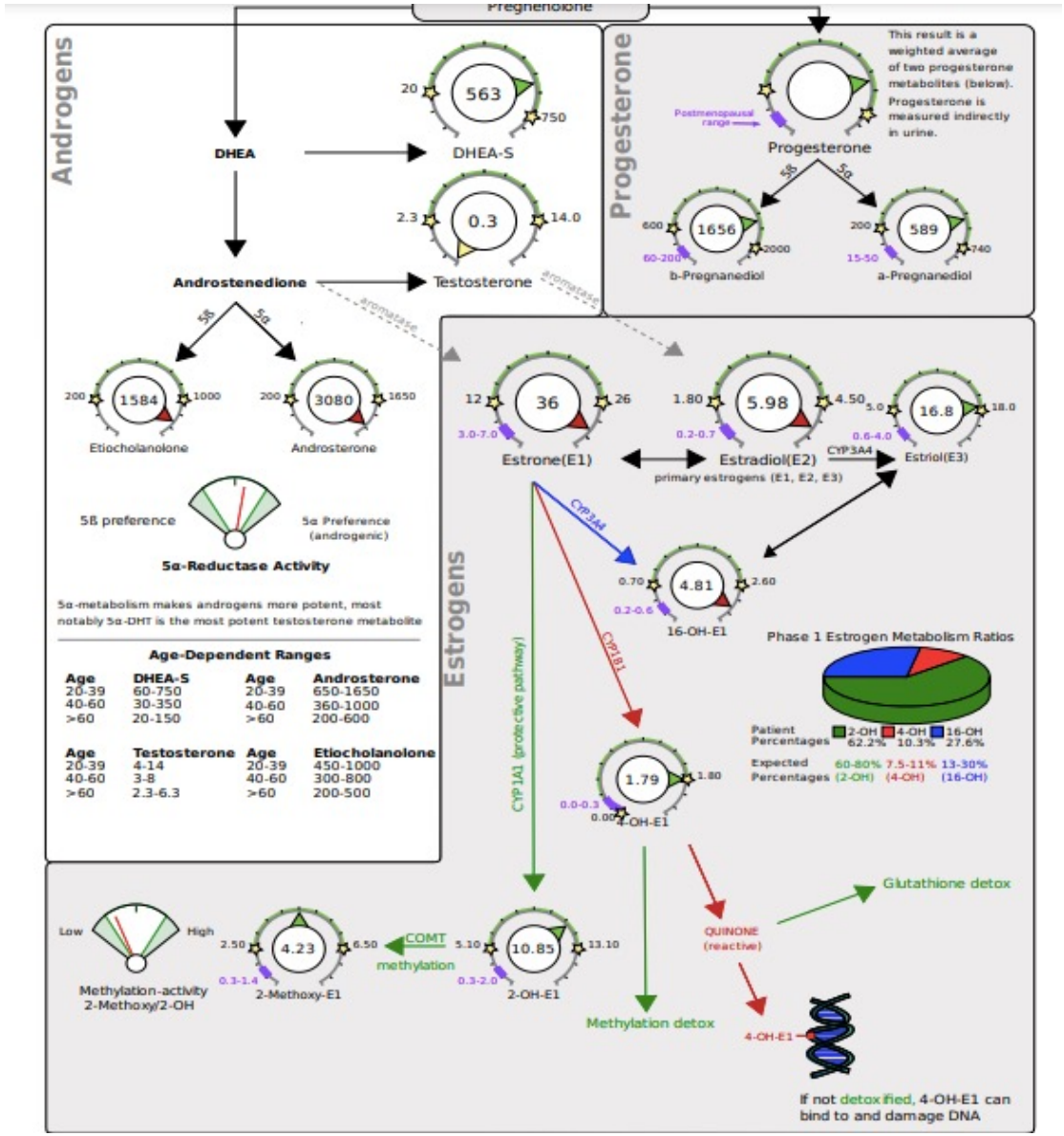
cortisol metabolism

Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

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

The following videos (which can also be found on the website under the listed names along with others) may aid your understanding:
DUTCH Plus Overview (quick overview) Estrogen Tutorial Female Androgen Tutorial Cortisol/CAR Tutorial

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



Organic Acid Tests (OATs)

Ordering Provider:
Jaclyn Smeaton ND

DOB: 1985-03-12
Age: 36
Gender: Female

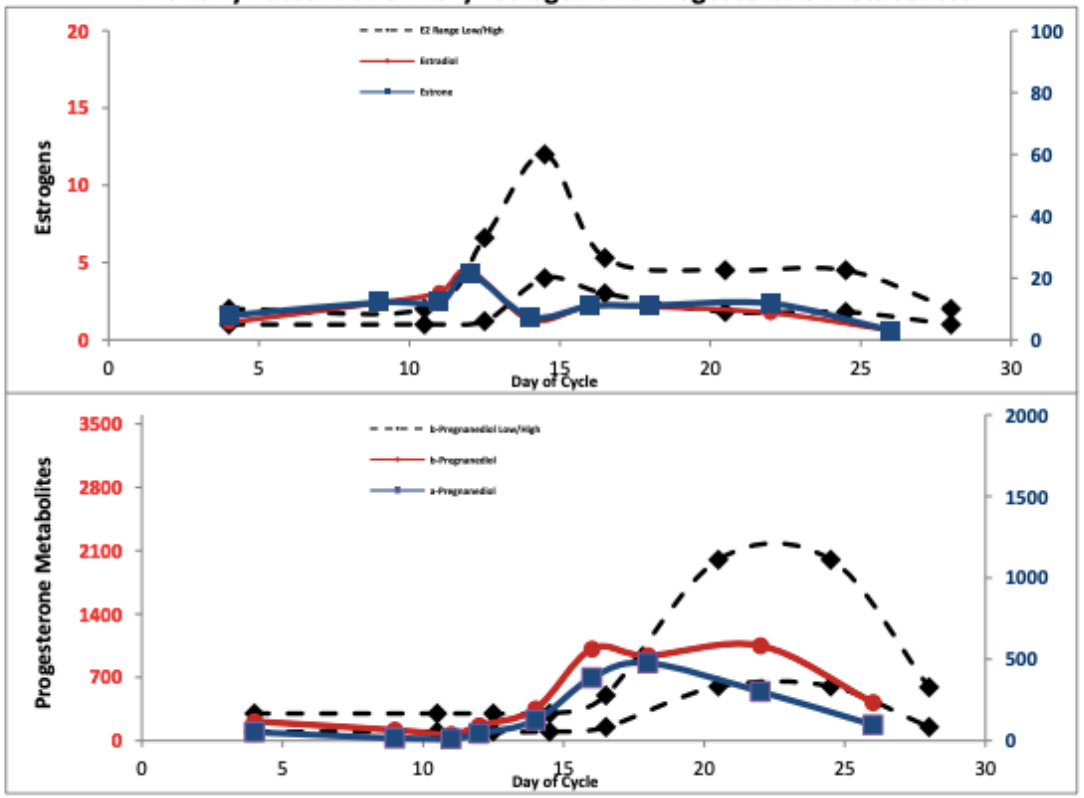
Last Menstrual Period:
2021-06-11

Collection Times:
2021-07-01 04:45AM (S)
2021-07-01 05:18AM (S)
2021-07-01 05:50AM (S)
2021-07-01 05:00PM (S)
2021-07-01 09:30PM (S)
2021-07-01 04:50AM (U)
2021-07-01 07:00AM (U)
2021-07-01 04:50PM (U)
2021-07-01 09:30PM (U)

Category	Test	Result	Units	Normal Range
Nutritional Organic Acids				
Vitamin B12 Marker (may be deficient if high) - (Urine)				
	Methylmalonate (MMA)	Within range	1.0	ug/mg	0 - 2.5
Vitamin B6 Markers (may be deficient if high) - (Urine)				
	Xanthurenate	Within range	0.20	ug/mg	0.12 - 1.2
	Kynurenate	Within range	1.4	ug/mg	0.8 - 4.5
Glutathione Marker (may be deficient if low or high) - (Urine)				
	Pyroglutamate	Within range	47.5	ug/mg	28 - 58
Neurotransmitter Metabolites				
Dopamine Metabolite - (Urine)				
	Homovanillate (HVA)	Low end of range	4.1	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite - (Urine)				
	Vanilmandelate (VMA)	Within range	2.9	ug/mg	2.2 - 5.5
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)				
	Melatonin* (Waking)	Above range	822.2	ng/mg	10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)				
	8-OHdG (Waking)	Within range	2.2	ng/mg	0 - 5.2

DUTCH - Cycle Mapping

Monthly Pattern of Urinary Estrogen and Progesterone Metabolites

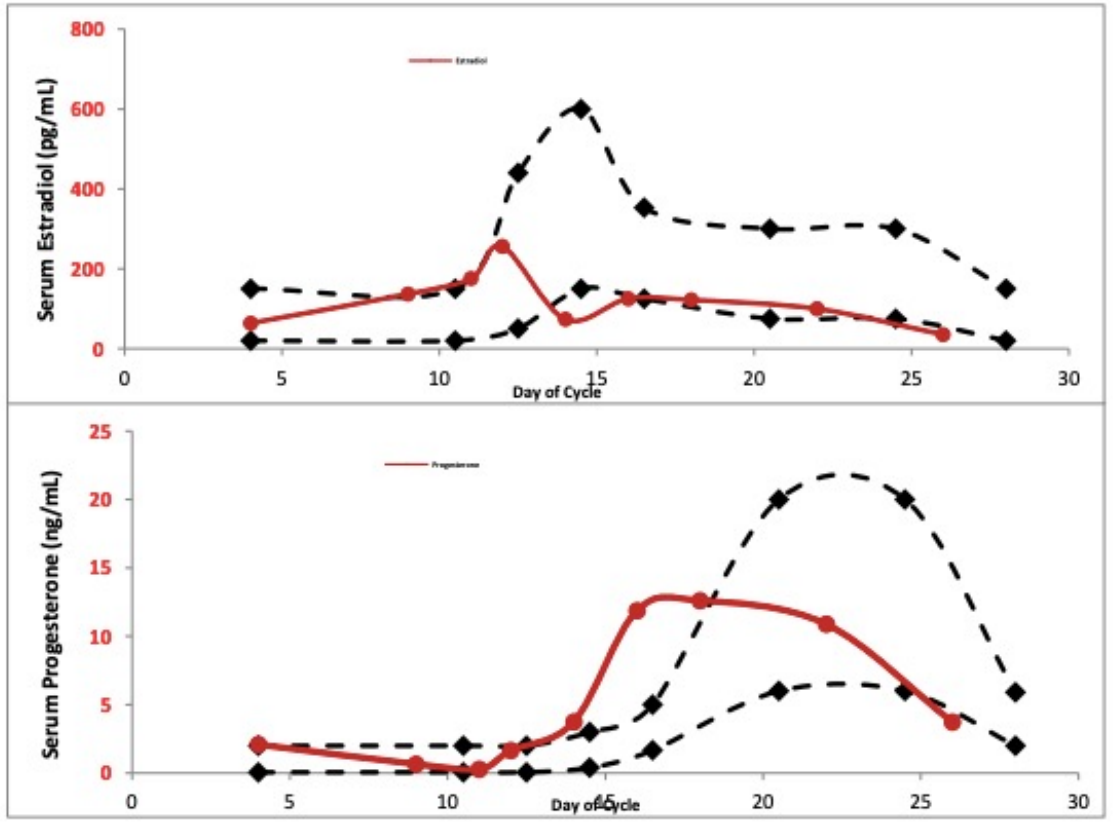


All values given in ng/mg creatinine

Measurement	1	2	3	4	5	6	7	8	9
Day of Cycle	4	9	11	12	14	16	18	22	26
Estradiol (E2)	1.1	2.4	3.1	4.5	1.3	2.2	2.1	1.7	0.6
Estrone (E1)	7.9	12.1	12.1	21.2	7.5	10.9	11.1	11.8	3.1
a-Pregnanediol	52	15	12	44	125	386	476	301	97
b-Pregnanediol	213	117	68	165	351	1014	939	1049	422
b-Pg / E2 Ratio	190	49	22	37	274	463	440	601	684

DUTCH - Cycle Mapping

Monthly Pattern of Estradiol and Progesterone - Serum Equivalent Estimates*



Measurement	1	2	3	4	5	6	7	8	9
Day of Cycle	4	9	11	12	14	16	18	22	26
Estradiol(pg/mL)	63.8	136.6	175.3	256.3	73.2	125.0	121.9	99.6	35.2
Progesterone(ng/mL)	2.1	0.7	0.3	1.7	3.8	11.9	12.6	10.9	3.7

Thank you!

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- **Additional Benefits Include:**
  - Easy At-Home Collection
  - Comprehensive Reporting Results
  - Drop-Ship to Your Patient's Doorstep
  - Quick Turn-Around Time on Lab Results
  - Dedicated Onboarding Concierge to Help Providers Get Started
  - Free Clinical Consults
  - Video Tutorials
  - Validated Peer-Reviewed Research

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