Casual Friday Series

The “Optimizing Hormones” Conversation Part 3

A Biogenetix Clinical Presentation

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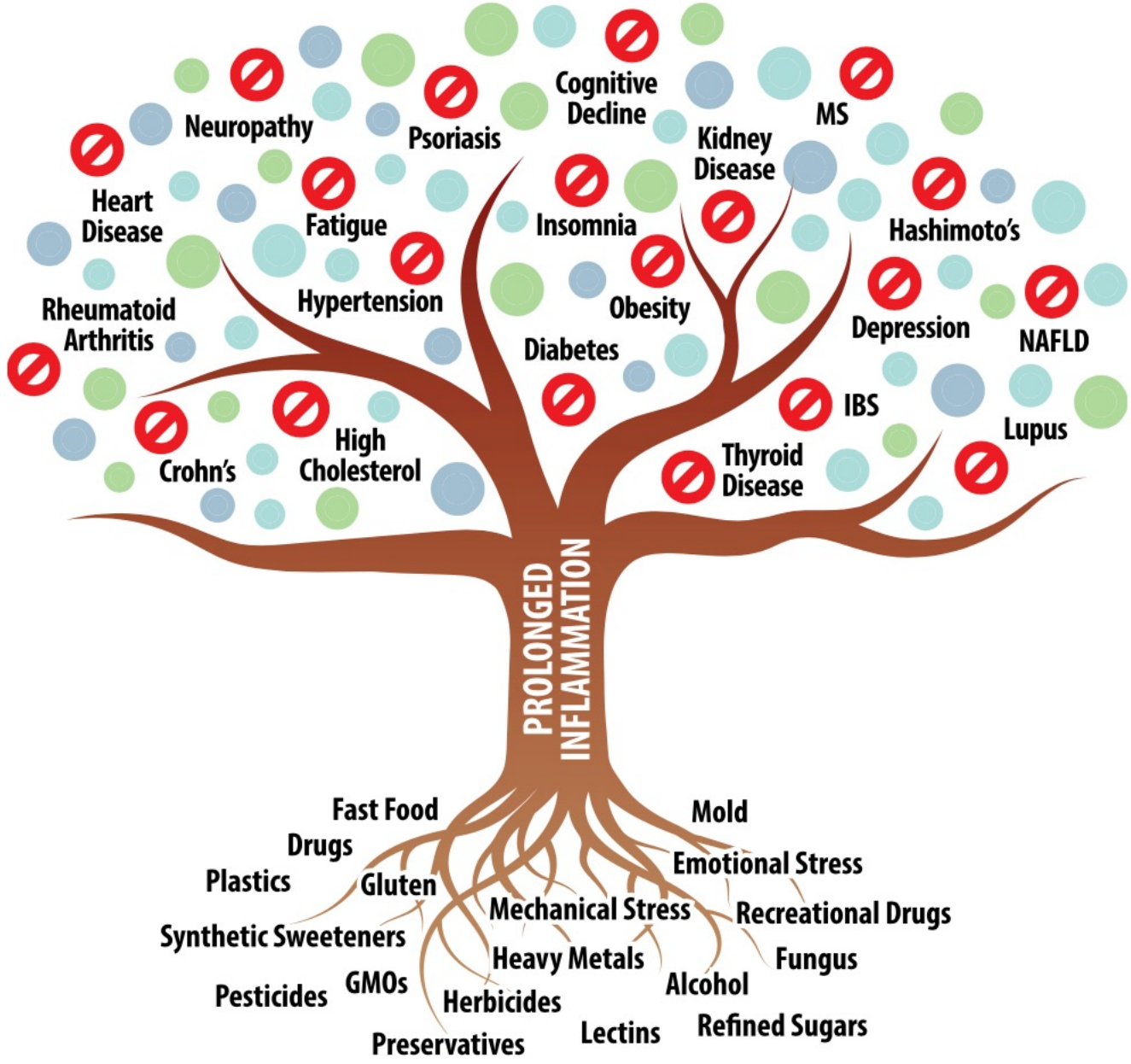
Disclaimer

- *Information in this presentation is not intended, in itself, to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*


Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
PROLONGED INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten
Mechanical Stress
Recreational Drugs
Synthetic Sweeteners
Heavy Metals
Fungus
Pesticides
GMOs
Herbicides
Alcohol
Lectins
Refined Sugars
Preservatives

Symptoms of hormonal imbalances that affect your metabolism include:

- Slow heartbeat or rapid heartbeat (tachycardia).
- Unexplained weight gain or weight loss.
- Fatigue.
- Constipation.
- Diarrhea or more frequent bowel movements.
- Numbness and tingling in your hands.
- Higher-than-normal blood cholesterol levels.
- Depression or anxiety.
- Being unable to tolerate cold temperatures or warm temperatures.
- Dry, coarse skin and hair.
- Thin, warm and moist skin.
- Irregular body fat distribution.
- Darkened skin in your armpit or the back and sides of your neck (acanthosis nigricans).
- Skin tags (small skin growths).
- Extreme thirst and frequent urination.

https://my.clevelandclinic.org/health/diseases/22673-hormonal-imbalance

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Open Access Review

Hypothalamic–Pituitary Diseases and Erectile Dysfunction

by Gianmaria Salvio *, Marianna Martino, Giulia Giancola, Giorgio Arnaldi † and Giancarlo Balercia †

Division of Endocrinology, Department of Clinical and Molecular Sciences (DISCLIMO), Polytechnic University of Marche, Umberto I Hospital, 60126 Ancona, Italy

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Several hormones contribute to ensure penile erection, a neurovascular phenomenon in which nitric oxide plays a major role. Erectile dysfunction (ED), which is defined as the persistent inability to obtain or maintain penile erection sufficient for a satisfactory sexual performance, may be due to arteriogenic, neurogenic, iatrogenic, but also endocrinological causes. The hypothalamus–pituitary axis plays a central role in the endocrine system and represents a fundamental link between the brain and peripheral glands, including gonads. Therefore, the hormonal production of the hypothalamic–pituitary axis can control various aspects of sexual function and its dysregulation can compromise erectile function. In addition, excess and deficiency of pituitary hormones or metabolic alterations that are associated with some pituitary diseases (e.g., Cushing's disease and acromegaly, hypopituitarism) can determine the development of ED with different mechanisms. Thus, the present review aimed to explore the relationship between

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All this, however, occurs thanks to the permissive role of androgens (mainly represented by testosterone, T) that regulate sexual behavior and male reproductive function in numerous ways. First of all, they influence the development of the male reproductive tract in early life and affect sexual behavior and libido in the adulthood [2]: sexual complaints are the most specific symptoms of T deficiency (hypogonadism) in adults [3] and can be reversed via T therapy [4]. T upregulates the activity of the enzyme NO synthase (NOS) by endothelial cells (eNOS) and NANC nerves (nNOS) and downregulates the activity of RhoA-ROCK (Ras homolog gene family member A-Rho-associated, coiled coil containing protein kinase), which is involved in the sensitization to calcium of penile smooth muscle cells, leading in both cases to vasodilation of the penile arteries [3].

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When one of the mechanisms described above is compromised, erectile dysfunction (ED), defined as the persistent inability to obtain or maintain penile erection sufficient for a satisfactory sexual performance [5], occurs. ED has a multifactorial etiology with vascular (due to arterial insufficiency or venous incompetency), neurogenic, endocrinological, or iatrogenic causes, but in most cases, it is determined by impaired penile blood flow due to atherosclerosis. As known, many cardiovascular risk factors are associated with ED, and there is a strong association between ED and the development of cardiovascular disease (CVD) [6]. The damage of endothelial cells, caused by numerous conditions such as hypertension, smoking, and diabetes, results in a reduction of NO released in the corpora cavernosa. In addition, low NOS activity is linked to ED, and it has been observed in conditions such as hypercholesterolemia, diabetes, and advanced age [7] as well as in hypogonadism [2], which is associated with increased cardiovascular mortality [8]. In this regard, several studies have documented an age-dependent reduction in circulating T levels in men (a condition named "Late-onset hypogonadism"—LOH) associated with sexual dysfunction and metabolic syndrome [9] and a recent meta-analysis confirmed that low T levels are a marker of cardiovascular risk in aging males [10]. In addition, chronic conditions such as liver cirrhosis, obesity, and hyperinsulinism may increase levels of sex hormone binding globulin (SHBG), which binds circulating T and limits its biological effects [3]. Despite this, the beneficial effects of T therapy on cardiovascular risk are still debated [11], while those on erectile function in patients with hypogonadism are widely recognized [4].

Table 1. Hypothalamic–pituitary diseases associated with erectile dysfunction and proposed mechanisms.

Dysfunction	Causes	Mechanisms
Pituitary Hormones Excess		
Hyperprolactinemia	Pituitary adenoma (prolactinoma) Sellar/parasellar masses Drugs Stalk effect	- Secondary hypogonadism due to disruption of GnRH pulsatility and gonadotropin secretion - Reduced libido due to direct effect on the central nervous system
Hypercortisolism	Corticotroph adenoma (Cushing's disease) Functional hypercortisolism	- Secondary hypogonadism due to disruption of GnRH pulsatility and gonadotropin secretion - Primary hypogonadism due to decreased number of Leydig cells in the testes - Endothelial dysfunction due to metabolic comorbidities
Acromegaly	Pituitary adenoma	- Secondary hypogonadism due to disruption of GnRH pulsatility and gonadotropin secretion. - Endothelial dysfunction due to metabolic comorbidities.
Hypopituitarism		
Hypogonadotropic hypogonadism	Pituitary adenoma Sellar/parasellar masses Drugs Functional hypogonadism TBI TNS Radiotherapy	- Reduced libido and dysregulation of sexual behavior - Endothelial dysfunction due to metabolic comorbidities - Reduced NO production in penile tissue due to reduced eNOS and nNOS activity
GHD	TBI TNS Radiotherapy	- Reduced NO production in penile tissue due to reduced nNOS activity
Hypocortisolism	TBI TNS Radiotherapy	- Unknown

GHD = growth hormone deficiency; NO = nitric oxide; TBI = traumatic brain injury; TNS = transsphenoidal surgery.

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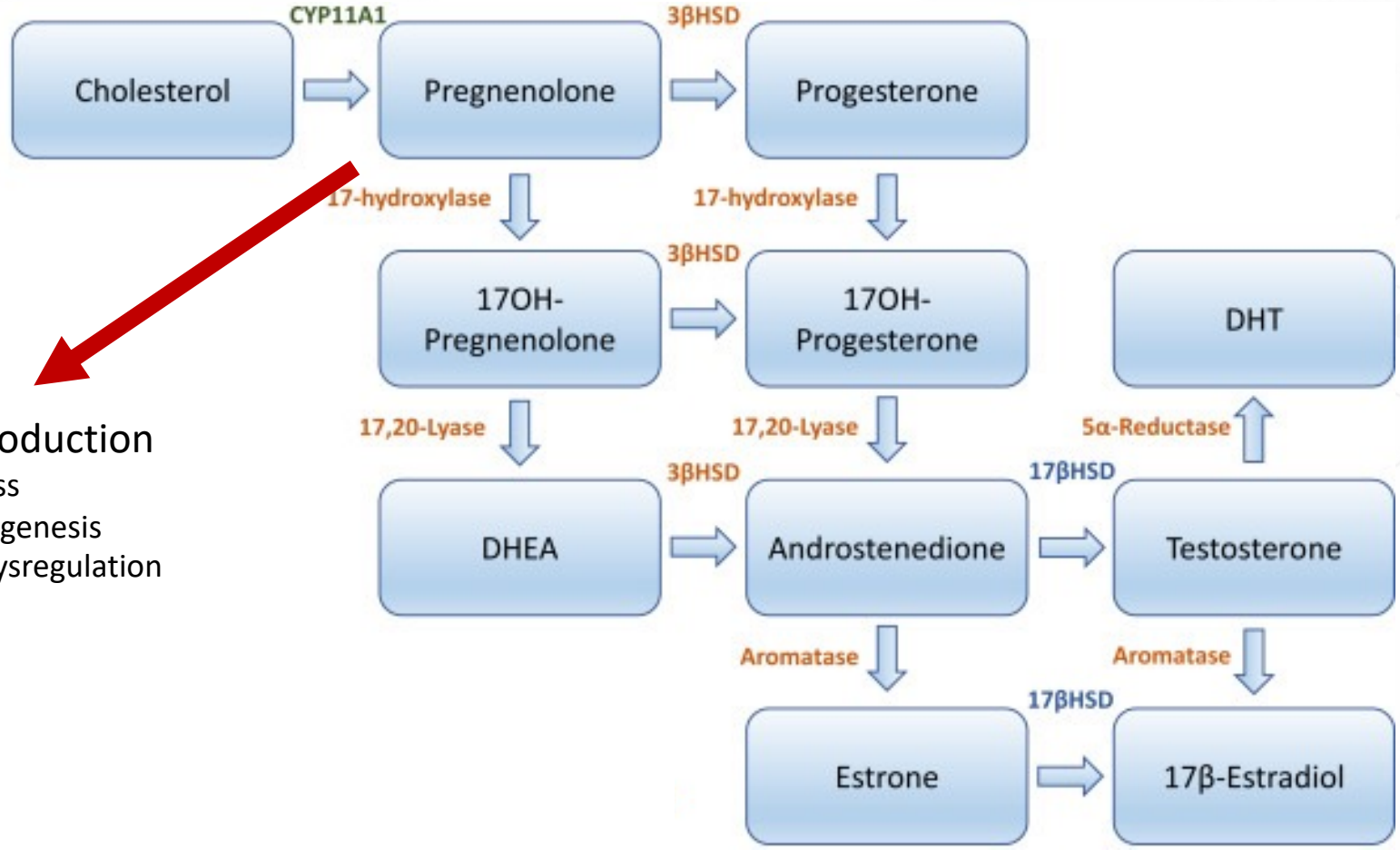
Although evidence suggests an important role for hypothalamic–pituitary hormones in the control of erectile function, the actual incidence of ED in pituitary disorders is poorly understood. Since ED presents an important effect on quality of life, as well as representing an early sign of endothelial dysfunction, it should always be investigated, preferably using validated questionnaires (e.g., IIEF-15 and SIEDY), and treated. In addition to the use of drugs with proven benefit on erectile function such as phosphodiesterase-5 inhibitors, the correction of all cardiovascular risk factors and the restoration of normal pituitary function appear essential in these patients.



Cortisol Production

- MCP stress
- Gluconeogenesis
- Inflam. Dysregulation
- Infection

69 yo, DM2, ED, Lantus, BP meds

Key (how to read the results):

Sex Hormones

Estradiol(E2)

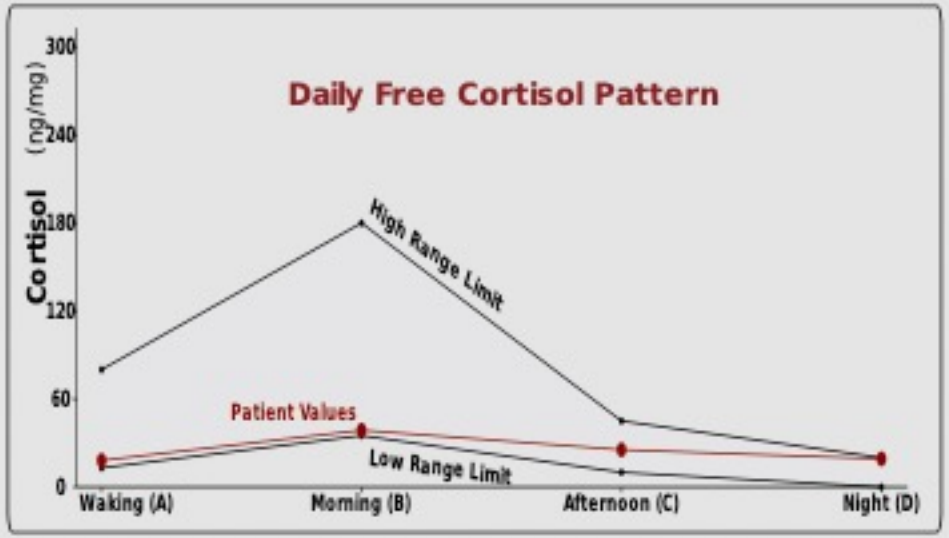
Testosterone

Testosterone

Age	Range
18-25	50-115
26-40	40-95
41-60	30-80
>60	25-60

Adrenal Hormones

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



Total DHEA Production

Age	Range
20-39	3000-5500
40-60	2000-4000
>60	1000-2500

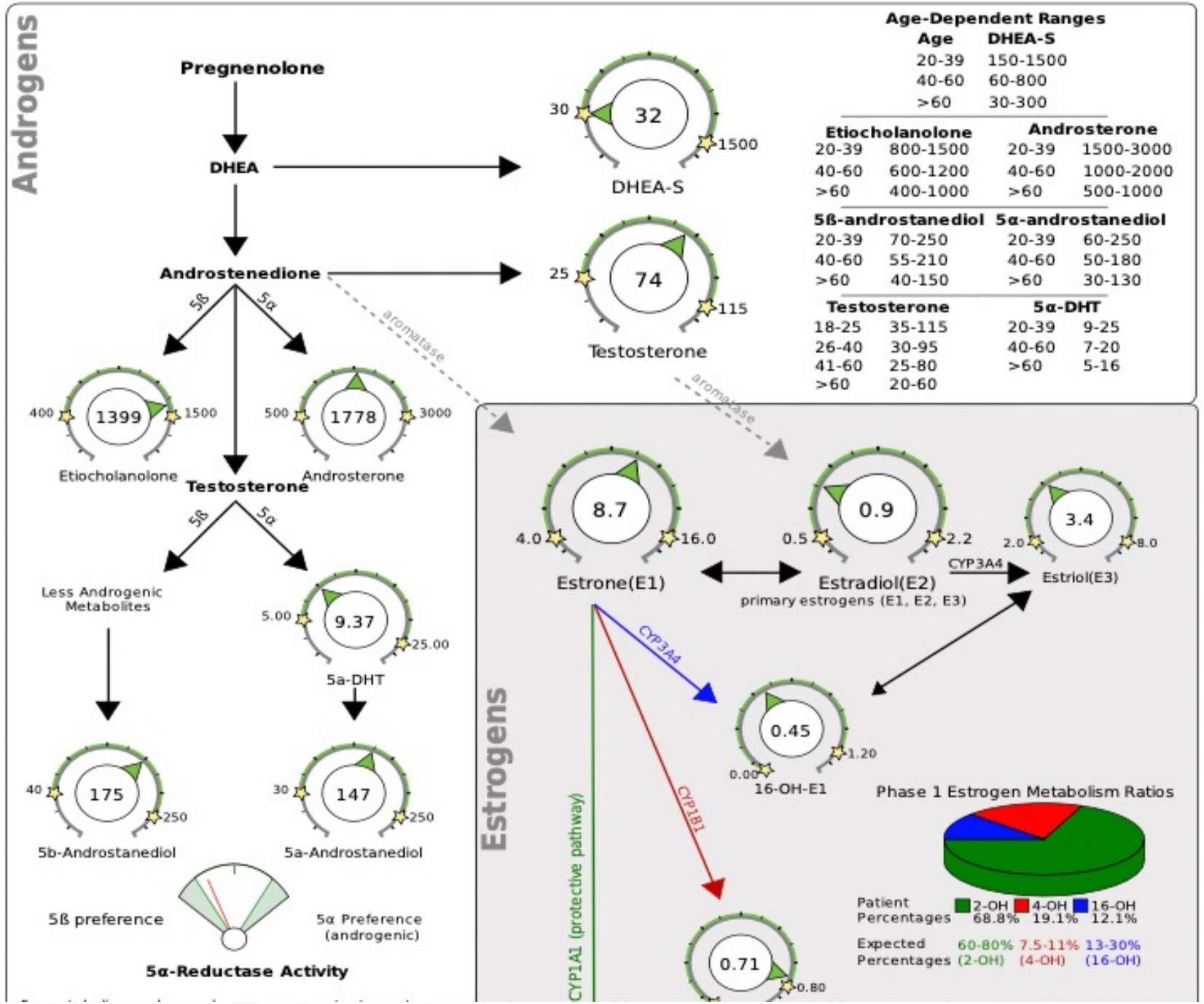
Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)

24hr Free Cortisol
(A+B+C+D)

cortisol metabolism

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

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


Androgens
Pregnenolone
DHEA
Androstenedione
5ß
5α
aromatase
aromatase
30
32
1500
DHEA-S
25
74
115
Testosterone
400
1399
1500
Etiocholanolone
500
1778
3000
Androsterone
Testosterone
5ß
5α
Less Androgenic Metabolites
5.00
9.37
25.00
5a-DHT
40
175
250
5b-Androstanediol
30
147
250
5a-Androstanediol
5ß preference
5α Preference (androgenic)
5α-Reductase Activity
Age-Dependent Ranges
Age DHEA-S
20-39 150-1500
40-60 60-800
>60 30-300
Etiocholanolone
20-39 800-1500
40-60 600-1200
>60 400-1000
Androsterone
20-39 1500-3000
40-60 1000-2000
>60 500-1000
5ß-androstanediol
20-39 70-250
40-60 55-210
>60 40-150
5α-androstanediol
20-39 60-250
40-60 50-180
>60 30-130
Testosterone
18-25 35-115
26-40 30-95
41-60 25-80
>60 20-60
5α-DHT
20-39 9-25
40-60 7-20
>60 5-16
Estrogens
4.0
8.7
16.0
Estrone(E1)
0.5
0.9
2.2
Estradiol(E2)
primary estrogens (E1, E2, E3)
CYP3A4
2.0
3.4
8.0
Estriol(E3)
CYP3A4
CYP1B1
0.00
0.45
1.20
16-OH-E1
CYP1A1 (protective pathway)
0.71
0.80
Phase 1 Estrogen Metabolism Ratios
Patient Percentages
2-OH 68.8%
4-OH 19.1%
16-OH 12.1%
Expected Percentages
60-80% (2-OH)
7.5-11% (4-OH)
13-30% (16-OH)

Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
Chemistries[01]					
▲ **Glucose**[01]	**166**	**High**		mg/dL	65-99
▲ **Hemoglobin A1c**[01]	**9.6**	**High**		%	4.8-5.6
Please Note:[01]					
	Prediabetes: 5.7 - 6.4				
	Diabetes: >6.4				
	Glycemic control for adults with diabetes: <7.0				
Uric Acid[01]	6.0			mg/dL	3.8-8.4
	Therapeutic target for gout patients: <6.0				

C-Peptide, Serum

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
C-Peptide, Serum[01]	2.9		ng/mL	1.1-4.4
	C-Peptide reference interval is for fasting patients.			

Insulin

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Insulin[01]	15.6		uIU/mL	2.6-24.9

	Cholesterol, Total [01]	162		mg/dL	100-199
	Triglycerides [01]	68		mg/dL	0-149
▼	**HDL Cholesterol** [01]	**35**	**Low**	mg/dL	>39
	VLDL Cholesterol Cal	13		mg/dL	5-40
▲	**LDL Chol Calc (NIH)**	**114**	**High**	mg/dL	0-99
	T. Chol/HDL Ratio	4.6		ratio	0.0-5.0
	Please Note: [01]				

T. Chol/HDL Ratio

	Men	Women
1/2 Avg.Risk	3.4	3.3
Avg.Risk	5.0	4.4
2X Avg.Risk	9.6	7.1
3X Avg.Risk	23.4	11.0

	C-Reactive Protein, Cardiac [01]	1.10	mg/L 0.00-3.00

Relative Risk for Future Cardiovascular Event

Low	<1.00
Average	1.00 - 3.00
High	>3.00

	Homocyst(e)ine [01]	12.2		umol/L	0.0-17.2

59 yo, DM2, BPH, ED, Metformin, BP meds, TH1 stimulants

Key (how to read the results):

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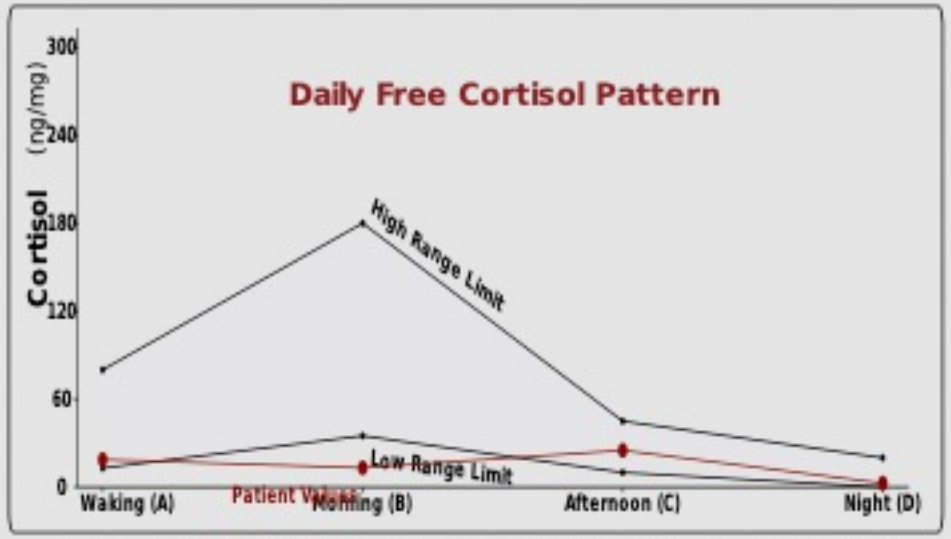

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24hr Free Cortisol
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(Total Cortisol Production)

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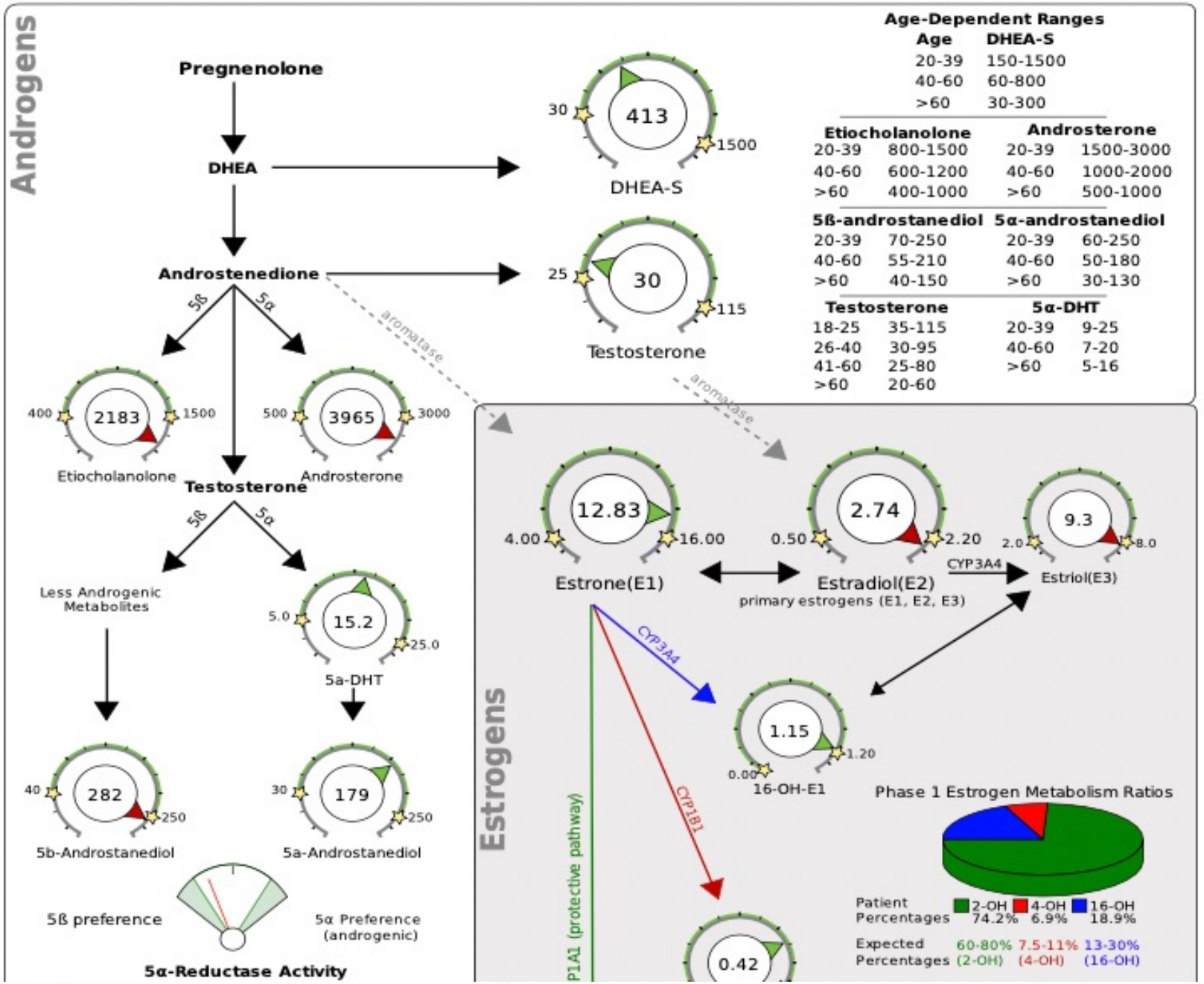
Androgens
Pregnenolone
DHEA
Androstenedione
5ß
5α
aromatase
413
30
1500
DHEA-S
30
25
115
Testosterone
2183
400
1500
Etiocholanolone
3965
500
3000
Androsterone
Testosterone
Less Androgenic Metabolites
15.2
5.0
25.0
5a-DHT
282
40
250
5b-Androstanediol
179
30
250
5a-Androstanediol
5ß preference
5α Preference (androgenic)
5α-Reductase Activity
Age-Dependent Ranges
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40-60 1000-2000
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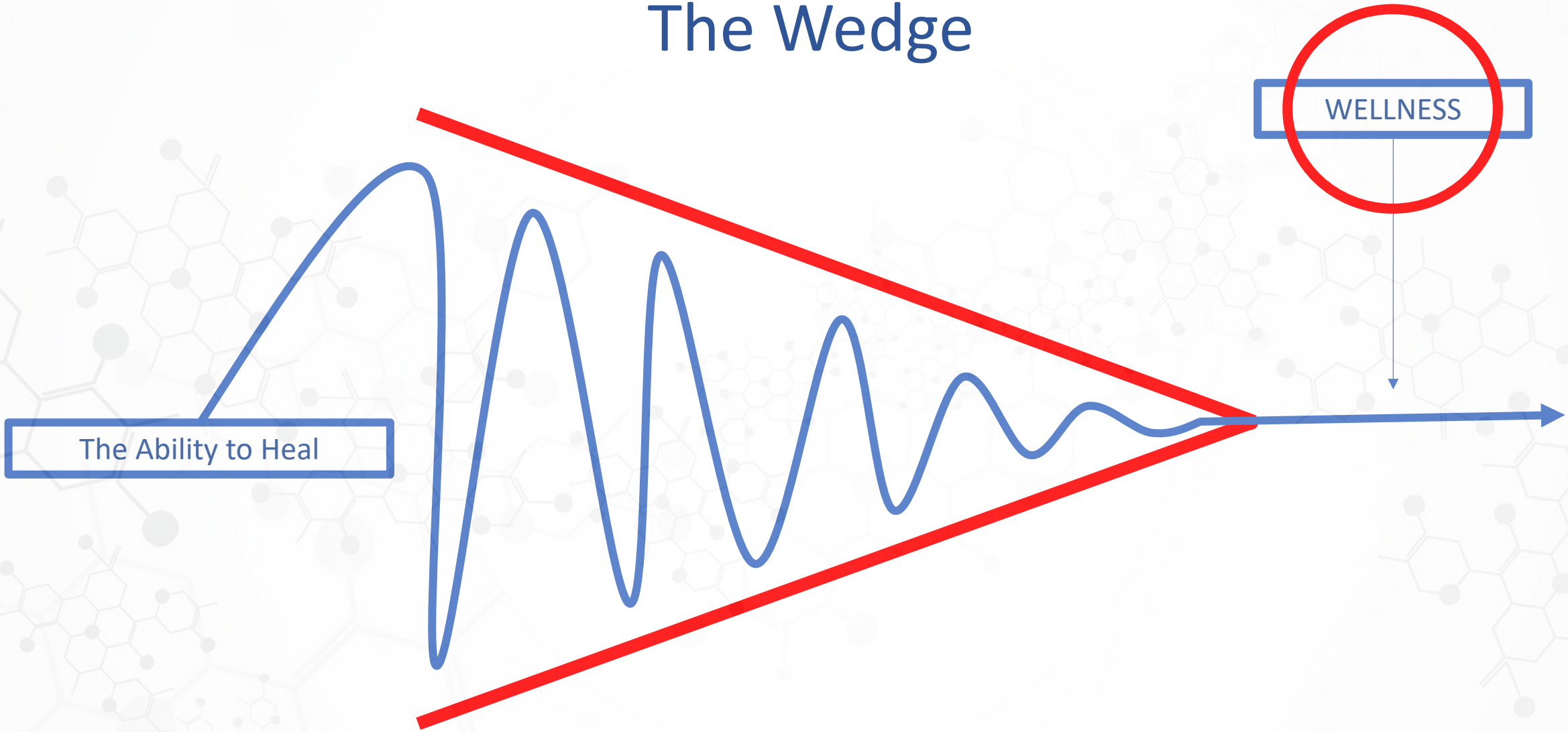
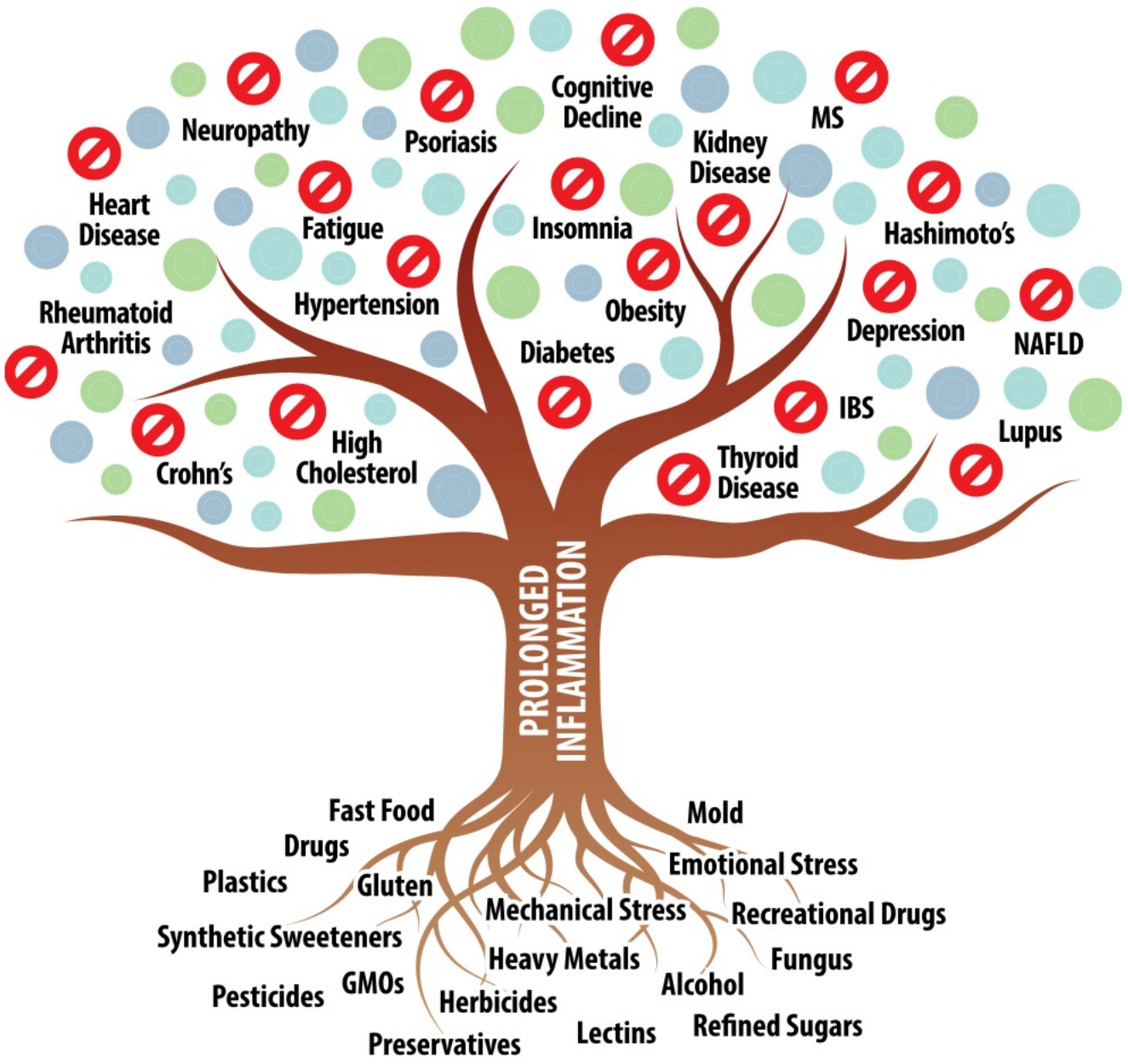
20-39 70-250
40-60 55-210
>60 40-150
5α-androstanediol
20-39 60-250
40-60 50-180
>60 30-130
Testosterone
18-25 35-115
26-40 30-95
41-60 25-80
>60 20-60
5α-DHT
20-39 9-25
40-60 7-20
>60 5-16
12.83
4.00
16.00
Estrone(E1)
2.74
0.50
2.20
Estradiol(E2)
9.3
2.0
8.0
Estriol(E3)
CYP3A4
primary estrogens (E1, E2, E3)
Estrogens
CYP3A4
CYP1B1
1.15
0.00
1.20
16-OH-E1
P1A1 (protective pathway)
0.42
Phase 1 Estrogen Metabolism Ratios
Patient Percentages
2-OH 74.2%
4-OH 6.9%
16-OH 18.9%
Expected Percentages
60-80% (2-OH)
7.5-11% (4-OH)
13-30% (16-OH)

	Test	Current Result and Flag		Previous Result and Date		Units	Reference Interval
	Chemistries [01]						
▲	**Glucose** [01]	**122**	**High**	**144**	03/17/2021	mg/dL	65-99
▲	**Hemoglobin A1c** [01]	**7.5**	**High**	**6.4**	03/17/2021	%	4.8-5.6
	Please Note: [01]						
		Prediabetes: 5.7 - 6.4					
		Diabetes: >6.4					
		Glycemic control for adults with diabetes: <7.0					
	Uric Acid [01]	5.2				mg/dL	3.0-7.2
		Therapeutic target for gout patients: <6.0					
	BUN [01]	9		9	03/17/2021	mg/dL	6-24
▲	**Creatinine** [01]	**1.13**	**High**	1.21*	03/17/2021	mg/dL	0.57-1.00
▼	**eGFR**	**56**	**Low**			mL/min/1.73	>59
▼	**BUN/Creatinine Ratio**	**8**	**Low**	**7***	03/17/2021		9-23
	Thyroid Peroxidase (TPO)						
▲	**Ab** [01]	**163**	**High**			IU/mL	0-34
	Thyroglobulin Antibody [01]	<1.0				IU/mL	0.0-0.9
		Thyroglobulin Antibody measured by Beckman Coulter Methodology					

Toxins Summary			
		Current	Previous Result
Environmental Toxins	Organochlorine pesticides		
	Organophosphate pesticides	Dimethylphosphate (DMP) ●, Diethylphosphate (DEP) ●, Dimethylthiophosphate (DMTP) ●	
	Other pesticides/herbcides		
	Phthalate Metabolites	mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) ●	
	Parabens		
	Acrylic Metabolites		
	Other Metabolites	Tiglylglycine (TG) ●	
	Alkylphenol	Bisphenol A (BPA) ●	
	Volatile Organic Compounds (VOCs)	2-Methylhippuric Acid (2MHA) ●	
	Urine Creatinine		
Mycotoxins V2	Aflatoxin	Aflatoxin B2 ●	
	Other	Ochratoxin A ●, Citrinin ●	
	Trichothecenes	diacetoxyscirpenol (DAS) ●	
	Urinary Creatinine		
Heavy Metals	Heavy Metals (Creatinine)	Barium ●	

The Wedge




Cognitive Decline
MS
Neuropathy
Psoriasis
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
High Cholesterol
Crohn's
Thyroid Disease
PROLONGED INFLAMMATION
Fast Food
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Drugs
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Synthetic Sweeteners
Heavy Metals
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