Casual Friday Series

The “Optimizing Hormones” Conversation

A Biogenetix Clinical Presentation

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Disclaimer

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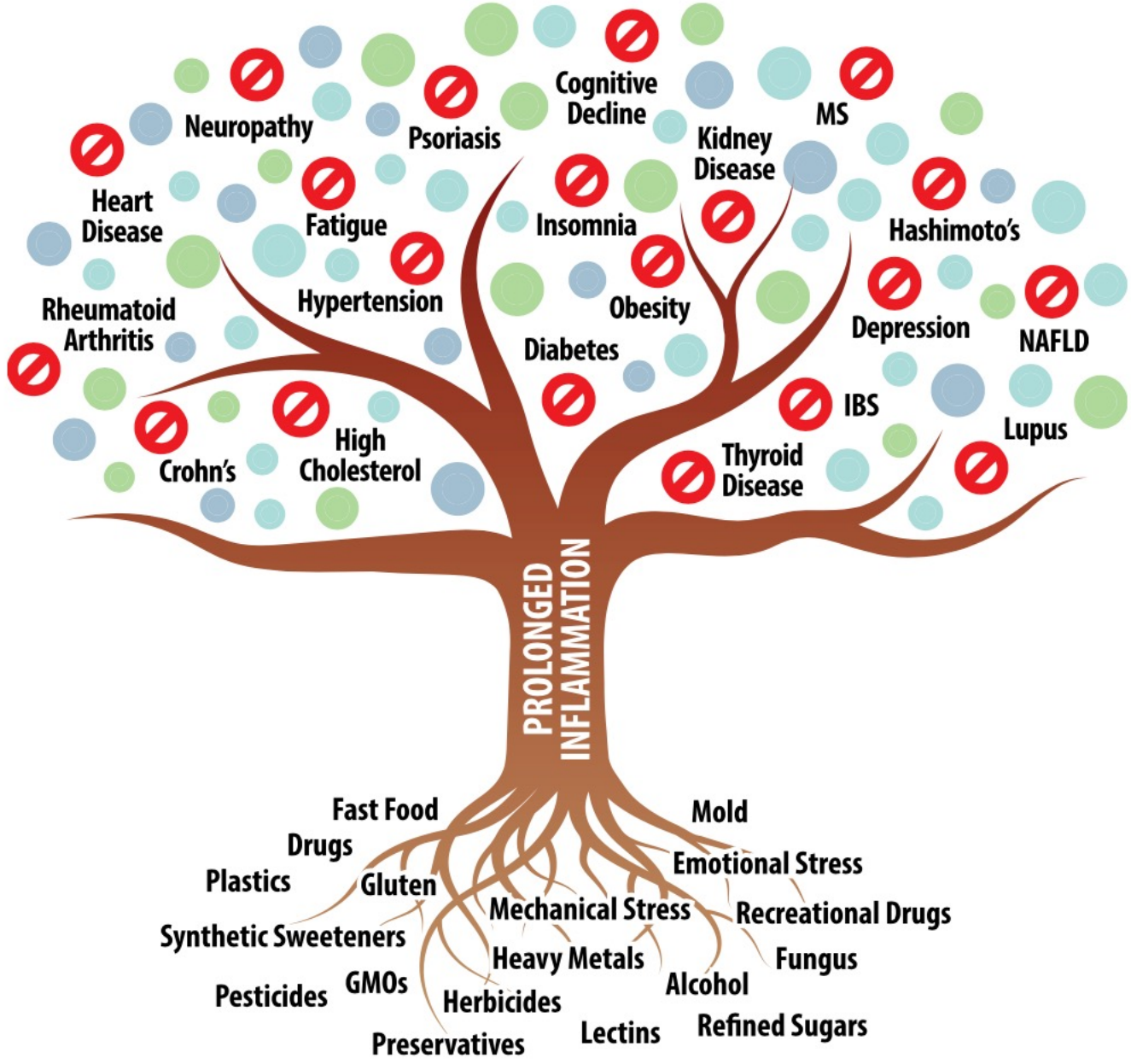
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
PROLONGED INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten
Mechanical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

Hormones are chemicals that coordinate different functions in your body by carrying messages through your blood to your organs, skin, muscles and other tissues. These signals tell your body what to do and when to do it. Hormones are essential for life and your health.

Scientists have identified over 50 hormones in the human body so far.

Hormones and most of the tissues (mainly glands) that create and release them make up your endocrine system. Hormones control many different bodily processes, including:

- Metabolism.
- Homeostasis (constant internal balance).
- Growth and development.
- Sexual function.
- Reproduction.
- Sleep-wake cycle.
- Mood.

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.

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Optimizing quality of life through sex steroids by their effects on neurotransmitters

Menopause-related symptoms such as hot flushes, night sweats, weight gain, and decreased sexual functioning all have negative impacts on quality of life and affect daily activities such as sleep, work, and leisure activities. During the menopause transition, neurotransmitters, neuropeptides, and neurosteroids undergo important changes as a consequence of the failure of gonadal hormone production, at a time when many central nervous system activities deteriorate. Sex hormones have been implicated in neurite outgrowth, synaptogenesis, dendritic branching, myelination, and other important mechanisms of neural plasticity. Knowledge of interactions between sex steroid hormones and the dominant neurotransmitters, such as serotonin, dopamine, GABA, and glutamate, will give women and health providers an important tool for improving their health and well-being. From the concept of neurosteroids derives another treatment strategy: the use of pharmaceutical agents that increase the synthesis of endogenous neurosteroids within the nervous system. This approach has so far been hampered by lack of knowledge concerning the regulation of the biosynthetic pathways of neurosteroids and their relationship with sex steroids produced by the peripheral gland or with exogenous steroids. The present review summarizes some of the available clinical and experimental findings supporting the critical role of neurosteroids in postmenopausal women and their impact on quality of life.

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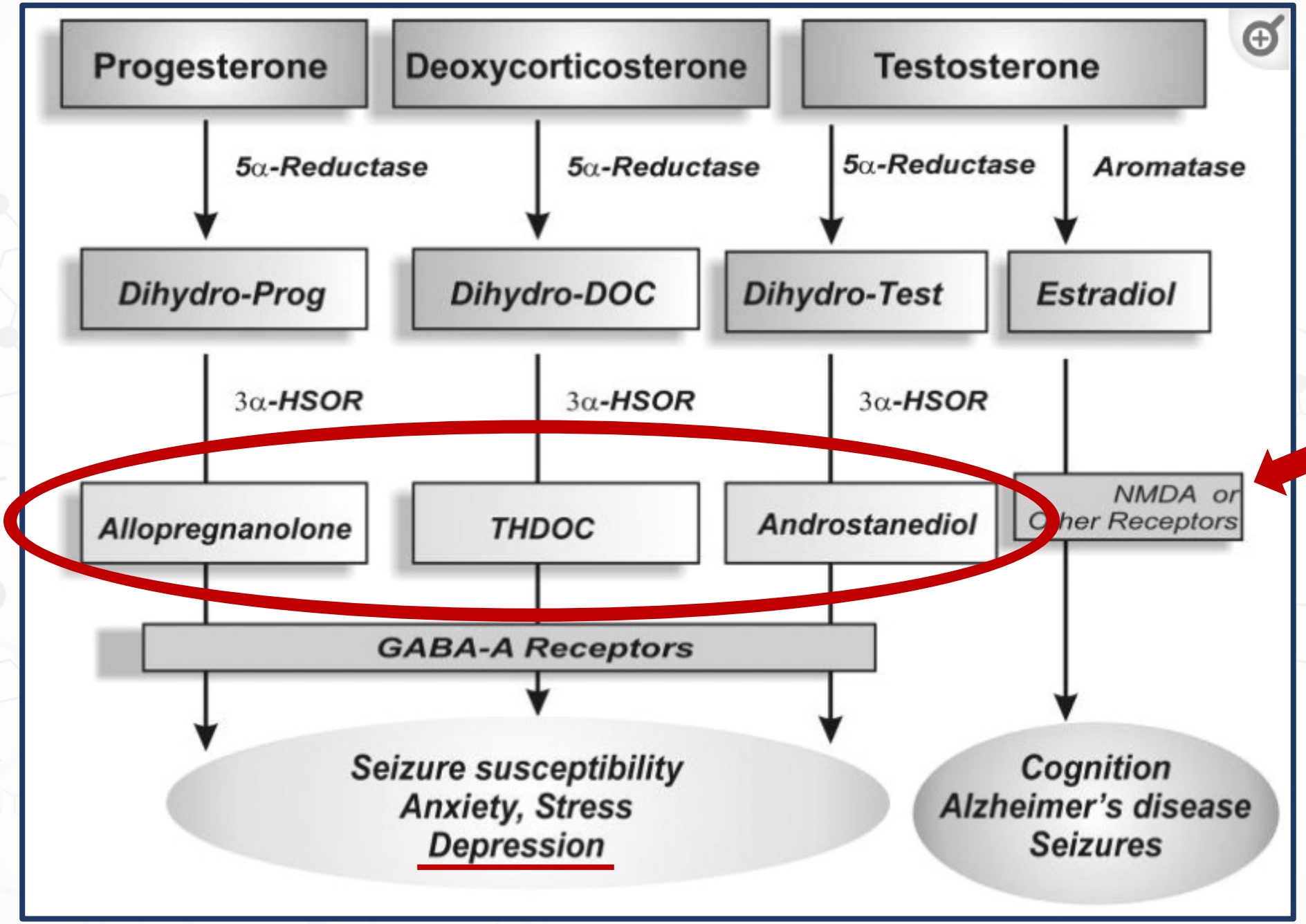
Neurosteroids: Endogenous Role in the Human Brian and Therapeutic Potentials

Neurosteroids are steroids synthesized within the brain and modulate neuronal excitability by rapid non-genomic actions. The term 'neurosteroids', originally coined by the French physiologist Etienne Baulieu, is now widely used to refer to steroids that are synthesized in the brain. Circulating steroid hormones serve as precursors for the synthesis of neurosteroids, which are produced locally in the hippocampus and other brain structures (Baulieu and Robel, 1990). Based on structural features, neurosteroids can be classified as pregnane neurosteroids, such as allopregnanolone and allotetrahydrodeoxycorticosterone (THDOC), androstane neurosteroids, such as androstanediol and etiocholanone, and sulfated neurosteroids, such as pregnenolone sulfate (PS) and dehydroepiandrosterone sulfate (DHEAS). Steroid hormones have long been recognized to have sedative, anesthetic and antiseizure properties in animals and humans (Aird, 1944; Aird and Gordan, 1951; Gyermek et al., 1967; Green et al., 1978). Studies during the past two decades have uncovered that progesterone and deoxycorticosterone serve as precursors for the endogenous neurosteroids allopregnanolone (5α-pregnane-3α-ol-20-one) and THDOC (5α-pregnane-3α,21-diol-20-one), respectively (Reddy, 2003; 2009a). Testosterone-derived androgens such as androstanediol (5α-androstane-3α,17β-diol) and estradiol can be considered as neurosteroids (Reddy, 2008). Generally, the acute effects of neurosteroids are not related to interactions with classical steroid hormone receptors that regulate gene transcription. Moreover, neurosteroids are not themselves active at intracellular steroid receptors. They modulate brain excitability primarily by interaction with neuronal membrane receptors and ion channels, principally GABA-A receptors (Lambert et al., 2003; Reddy, 2003; Akk et al., 2009). Neurosteroids are endogenous regulators of neuronal excitability, and therefore provide tremendous opportunities for developing therapeutic approaches (Reddy and Kulkarni, 2000; Morrow, 2007). This chapter reviews the



Glutamate Receptor

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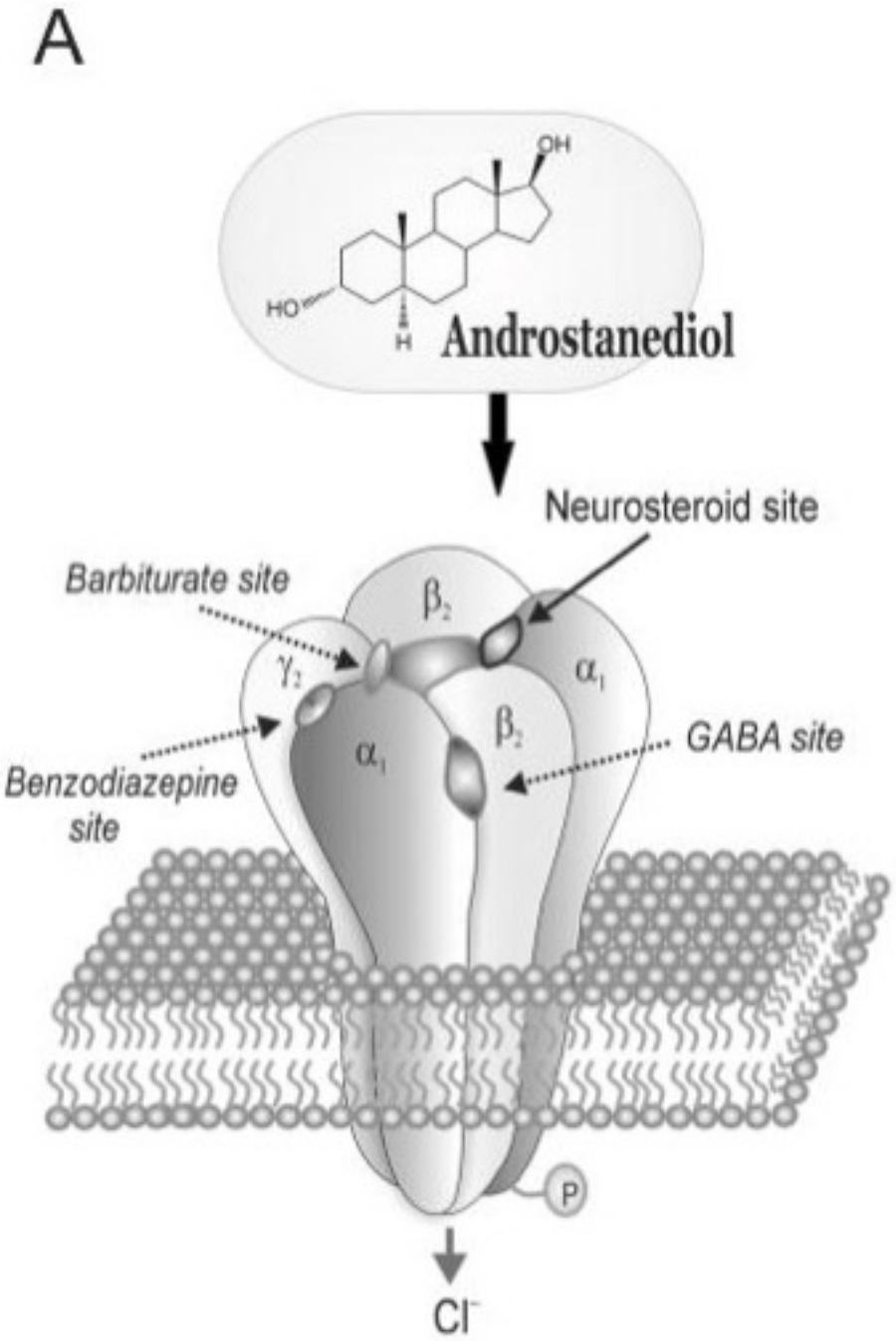
(sedatives)

(Xanax, Valium) Tranquilizers



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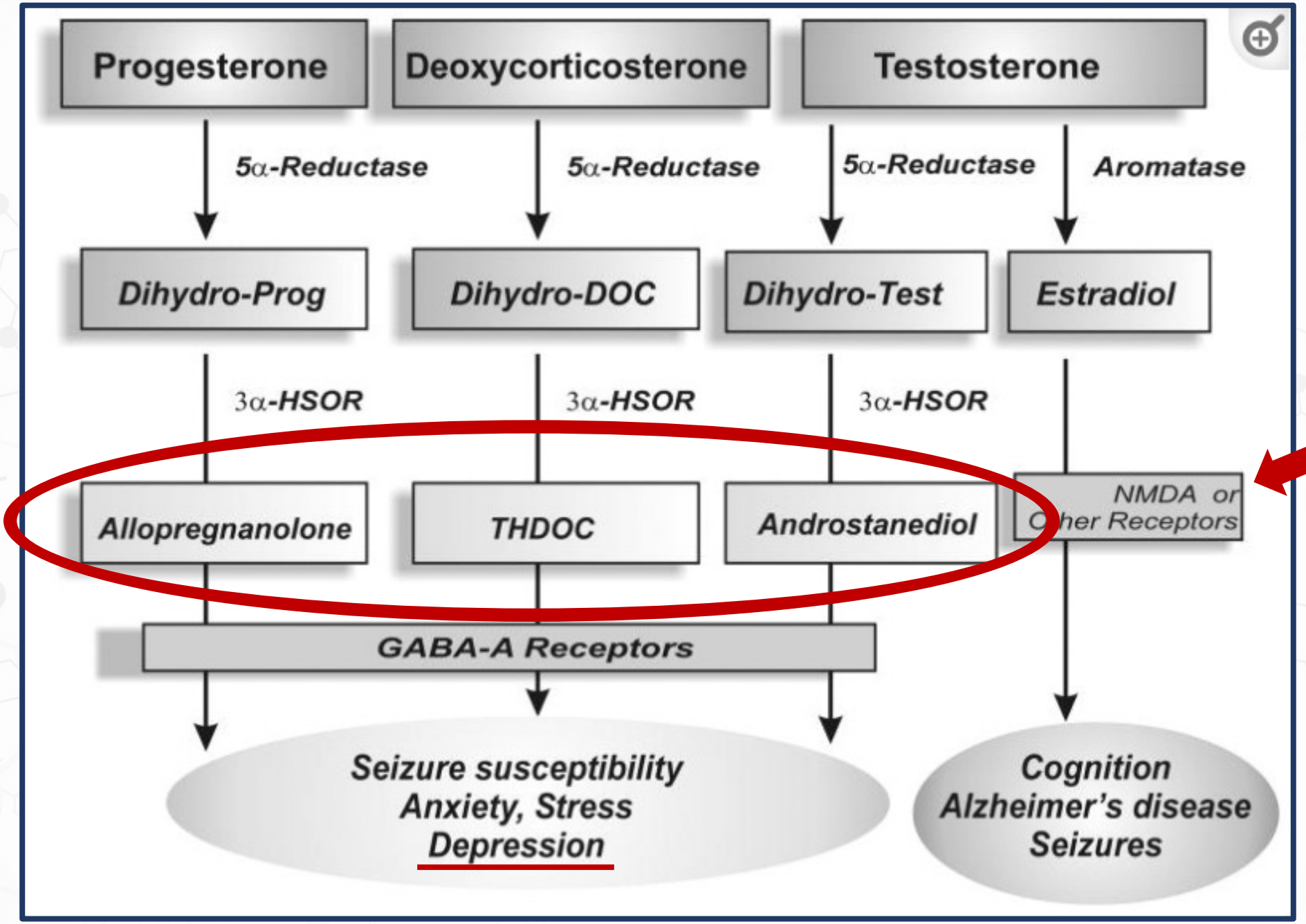

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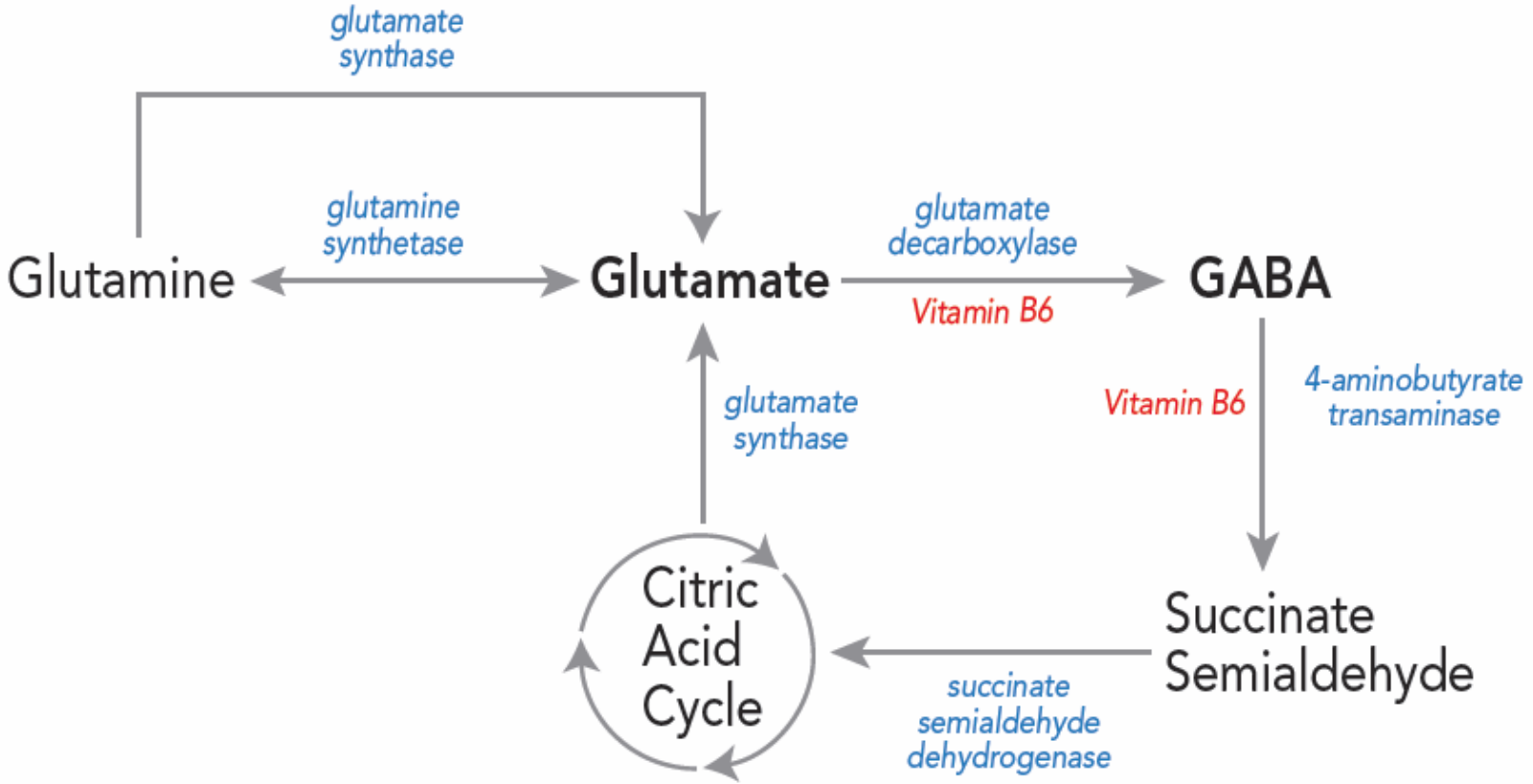

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Neurosteroids: Endogenous Role in the Human Brian and Therapeutic Potentials

Doc

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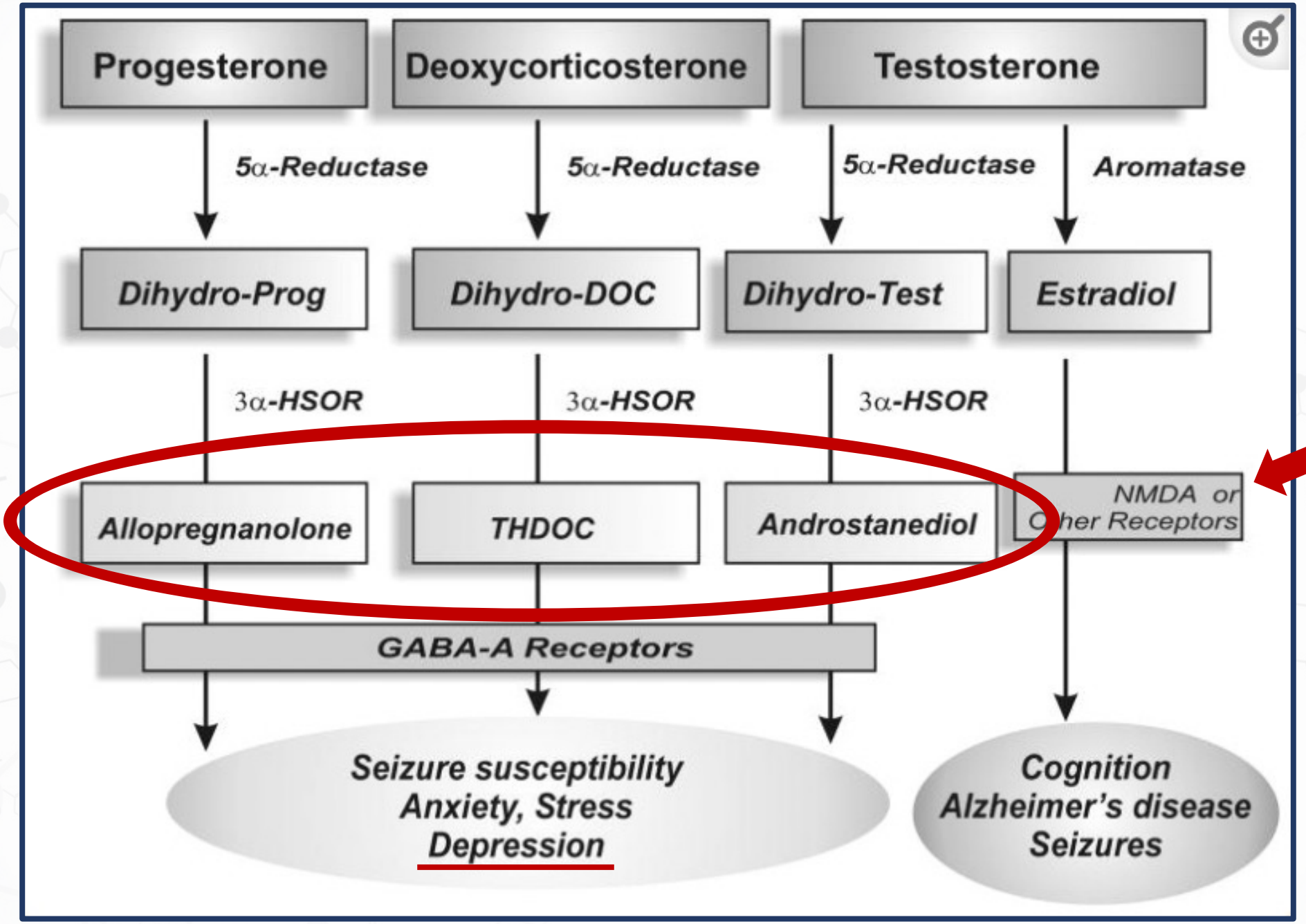
Anxiety

There is considerable evidence for an involvement of neurosteroids in the etiology of anxiety disorders. Neurosteroids such as allopregnanolone and THDOC are potent anxiolytic agents (Crawley et al., 1986; Bitran et al., 1995; Wieland et al., 1995; Reddy and Kulkarni, 2000; Finn et al., 2003; Eser et al., 2008; Maguire et al., 2005). Progesterone also has anxiolytic activity in animal models (Reddy and Kulkarni, 1997). Administration of progesterone produces similar sedative-anxiolytic effects in men and women (Soderpalm et al., 2004). The allopregnanolone- and progesterone-induced anxiolytic effects can be blocked by picrotoxin (Reddy and Kulkarni, 1997), suggesting that GABA-A receptors mediate the anxiolytic properties of neurosteroids. Anxiolytic properties have also been demonstrated with the use of synthetic analogs of allopregnanolone (Vanover et al., 2000). Treatment with fluoxetine, a specific serotonin uptake inhibitor, dose-dependently increases brain allopregnanolone levels (Uzunov et al., 1996), suggesting that elevated neurosteroid synthesis could be involved in the anxiolytic and antidysphoric actions of fluoxetine. In patients with induced panic attacks, there is pronounced decrease in allopregnanolone levels, and elevated neurosteroids may counteract the occurrence of spontaneous panic attacks (Strohle et al., 2000; 2003). Therefore, replacement of neurosteroids by synthetic analogs or stimulation of endogenous neurosteroid synthesis might constitute a promising novel strategy for the treatment of anxiety disorders.

Table 1

Pharmacological profile of major neurosteroids.

Neurosteroid	Pharmacological Actions	Mechanism of Action
Allopregnanolone	Sedative-hypnotic Anxiolytic, anticonvulsant Antistress, neuroprotection	Potentiation of GABA-A receptor function
THDOC	Sedative-hypnotic Anxiolytic, anticonvulsant Antistress, neuroprotection	Potentiation of GABA-A receptor function
Androstanediol	Anxiolytic, anticonvulsant	Potentiation of GABA-A receptor function
Pregnenolone sulfate	Anxiogenic, proconvulsant Memory enhancing, neuroprotection	Inhibition of GABA-A receptor function Enhanced NMDA receptor function
Dehydroepiandrosterone sulfate	Anxiogenic, proconvulsant Memory enhancing Neurogenesis, neuroprotection	Inhibition of GABA-A receptor function Enhanced NMDA receptor function Anti-glucocorticoid action



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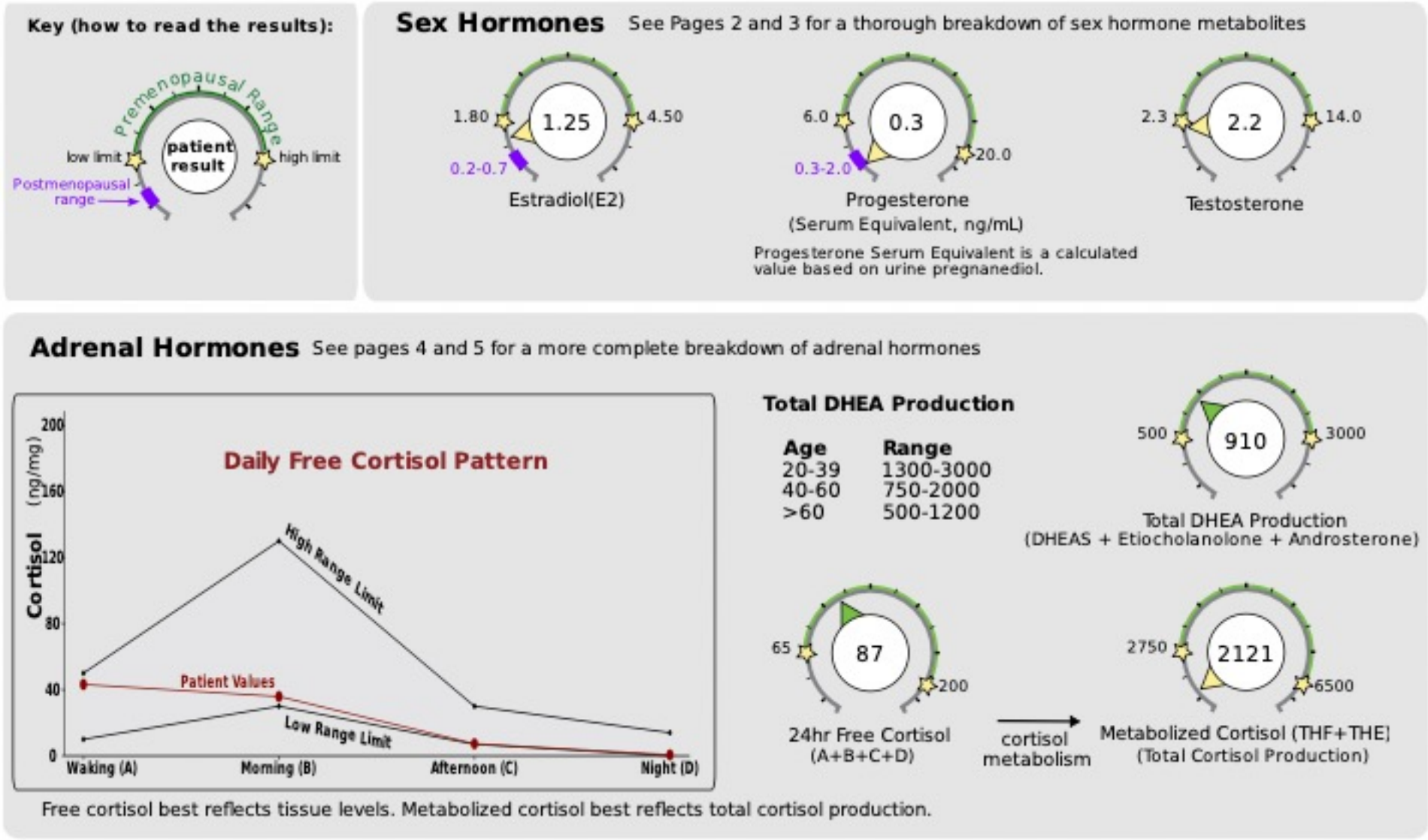
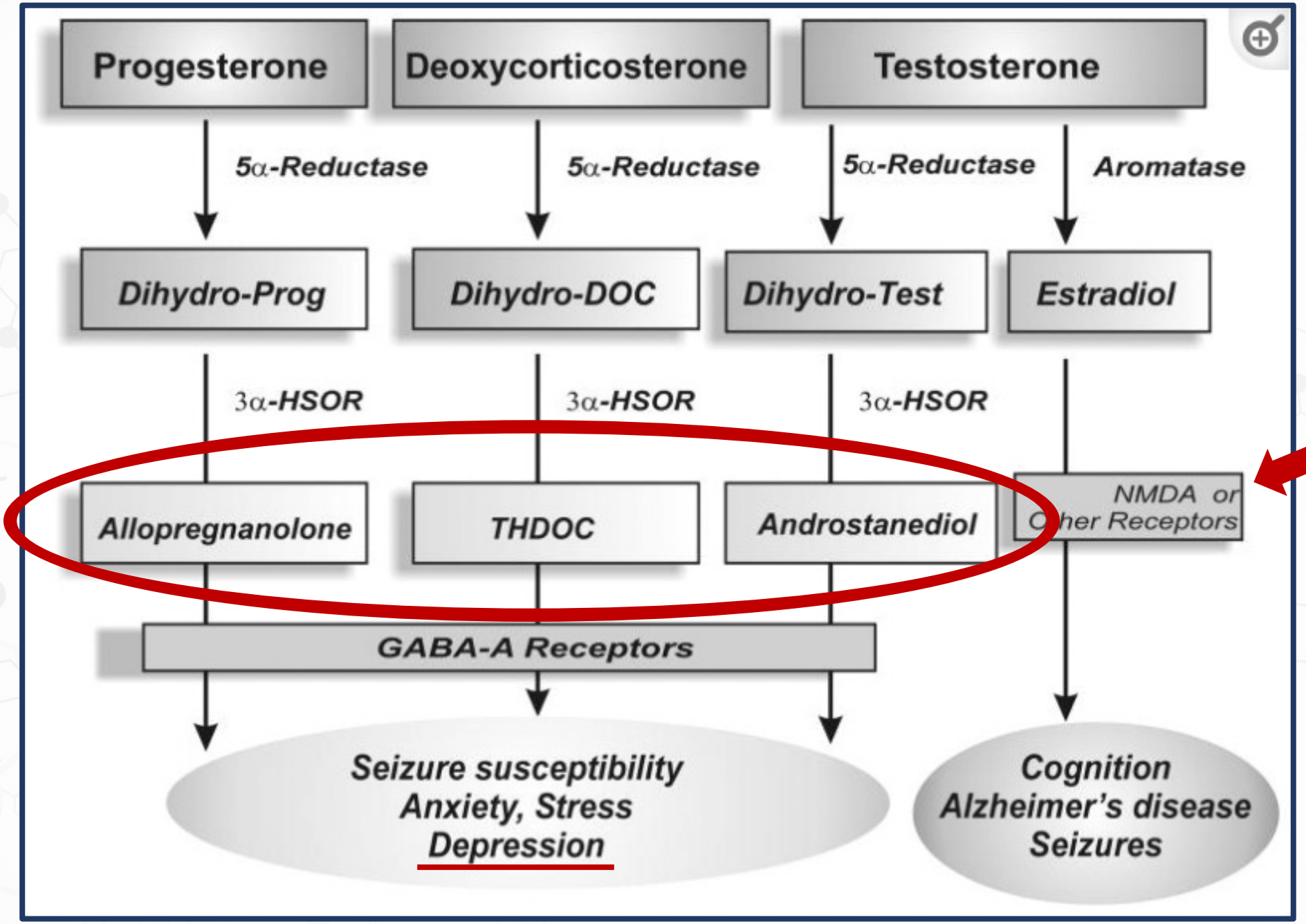
32 yo female on SSRI and BC





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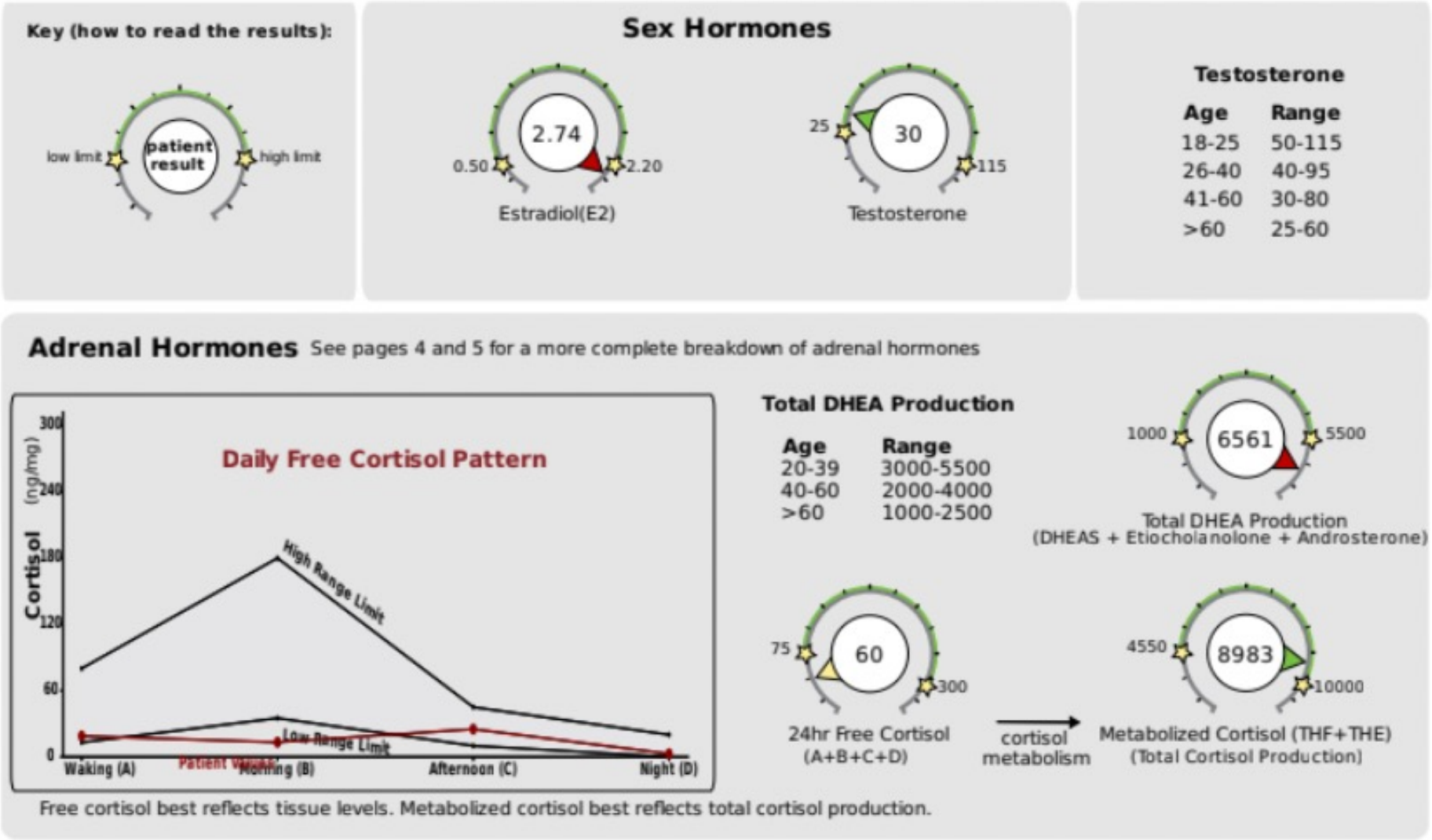
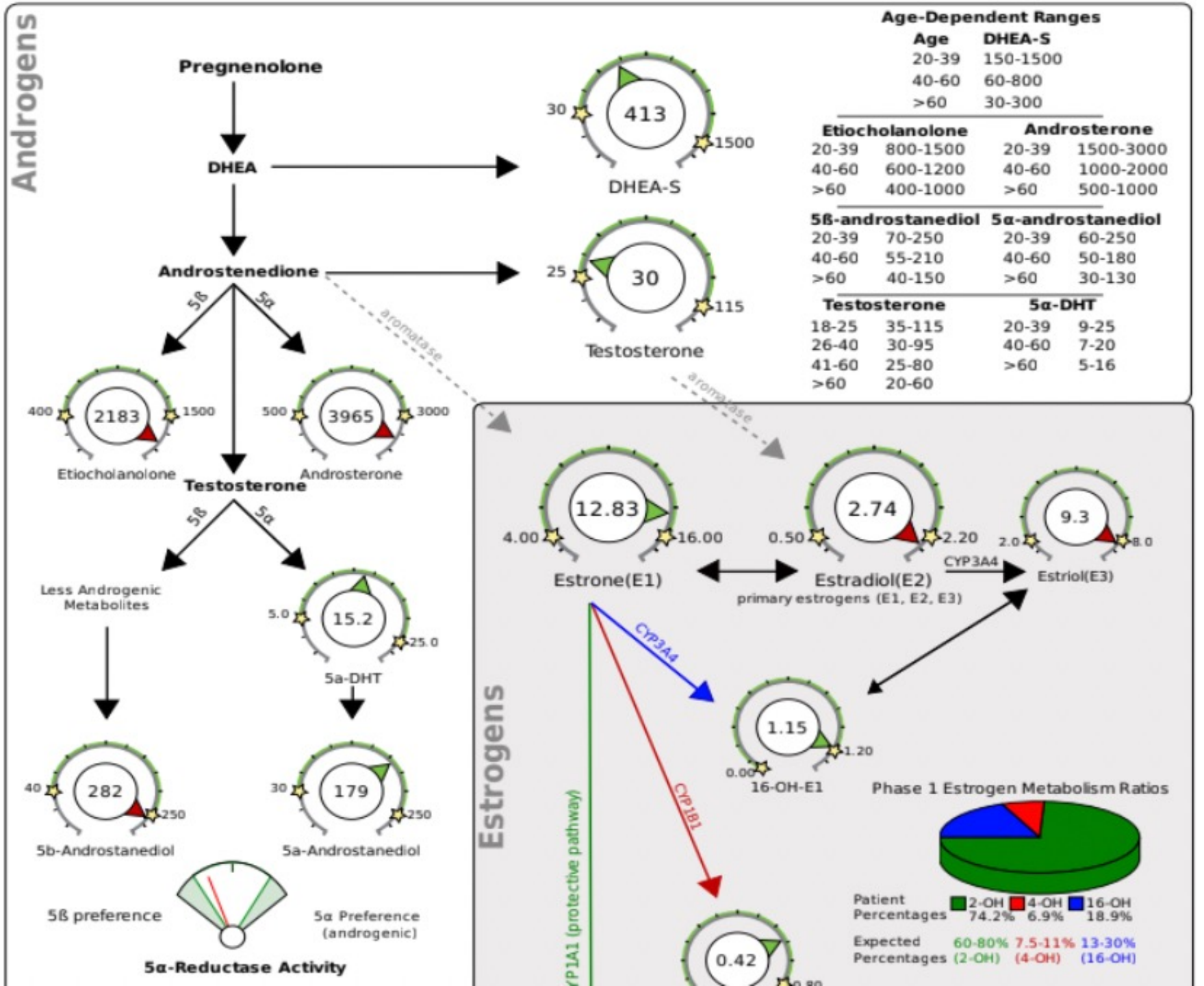
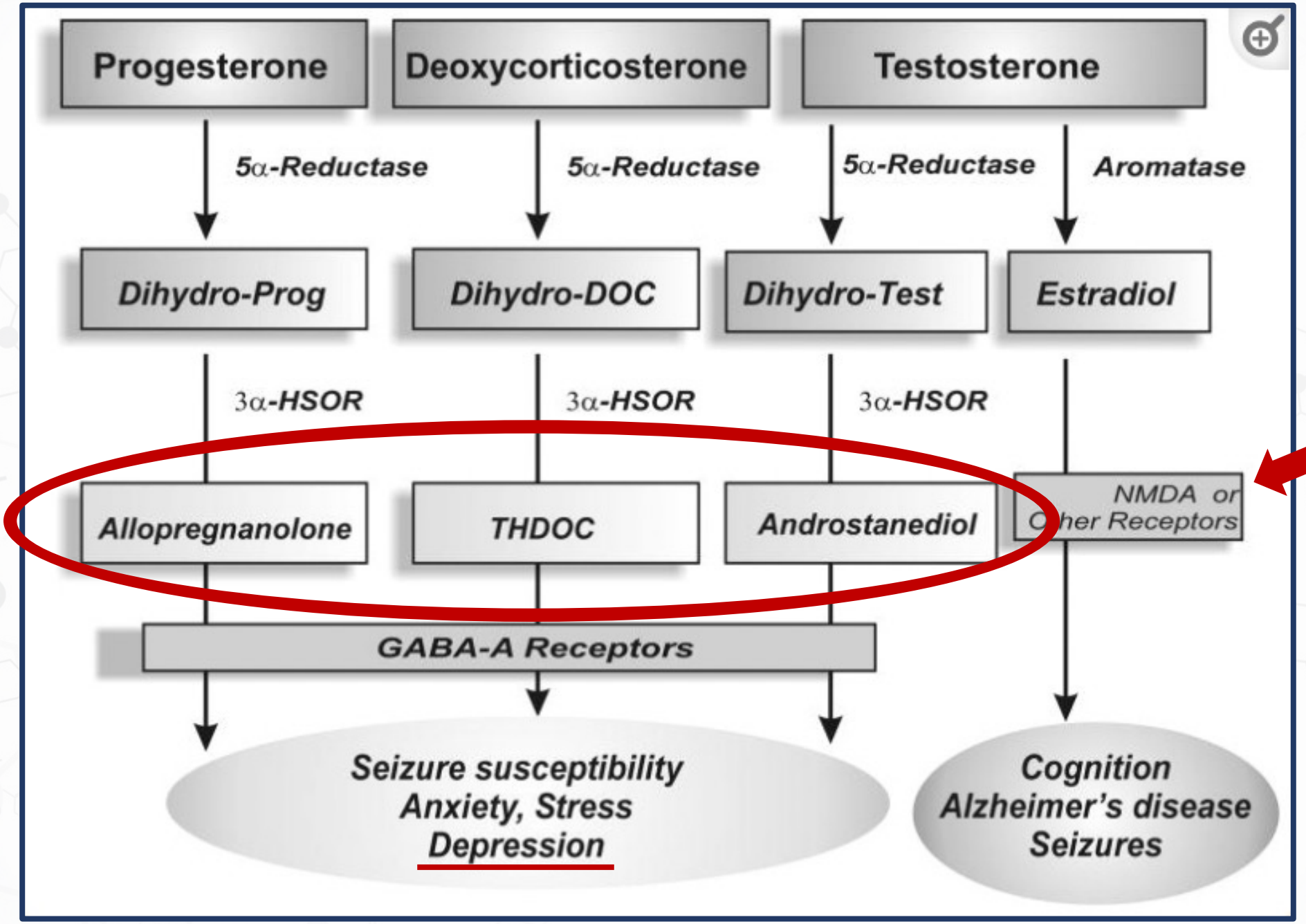
59 yo male dm2 anxiety, depression, SSRI, DHEA




Androgens
Pregnenolone
DHEA
Androstenedione
Testosterone
5ß
5α
aromatase
413
30
1500
DHEA-S
30
25
115
Testosterone
2183
400
1500
Etiocholanolone
3965
500
3000
Androsterone
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
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
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)
CYP3A4
CYP1B1
CYP1A1 (protective pathway)
1.15
0.00
1.20
16-OH-E1
0.42
0.80
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)



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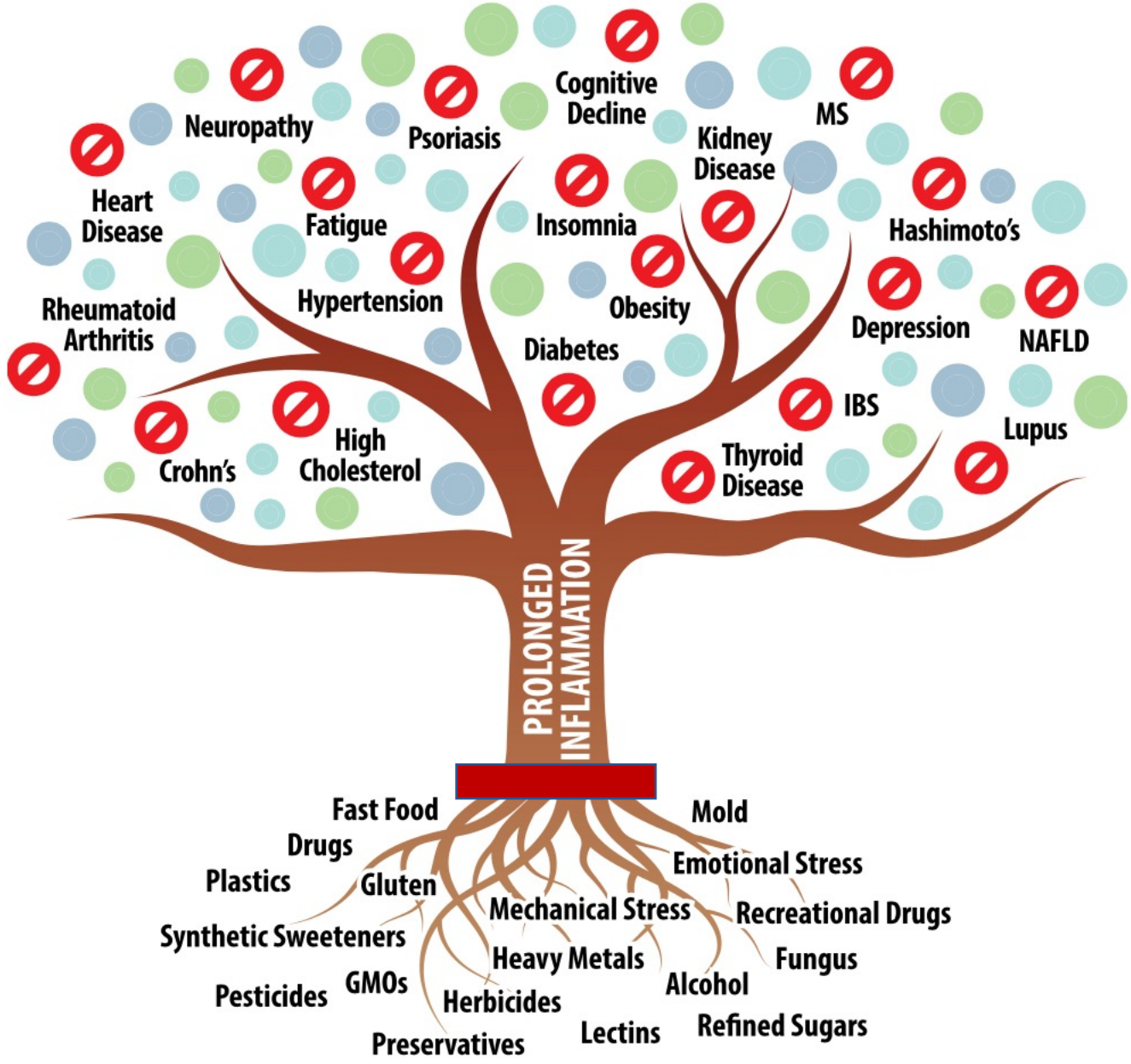
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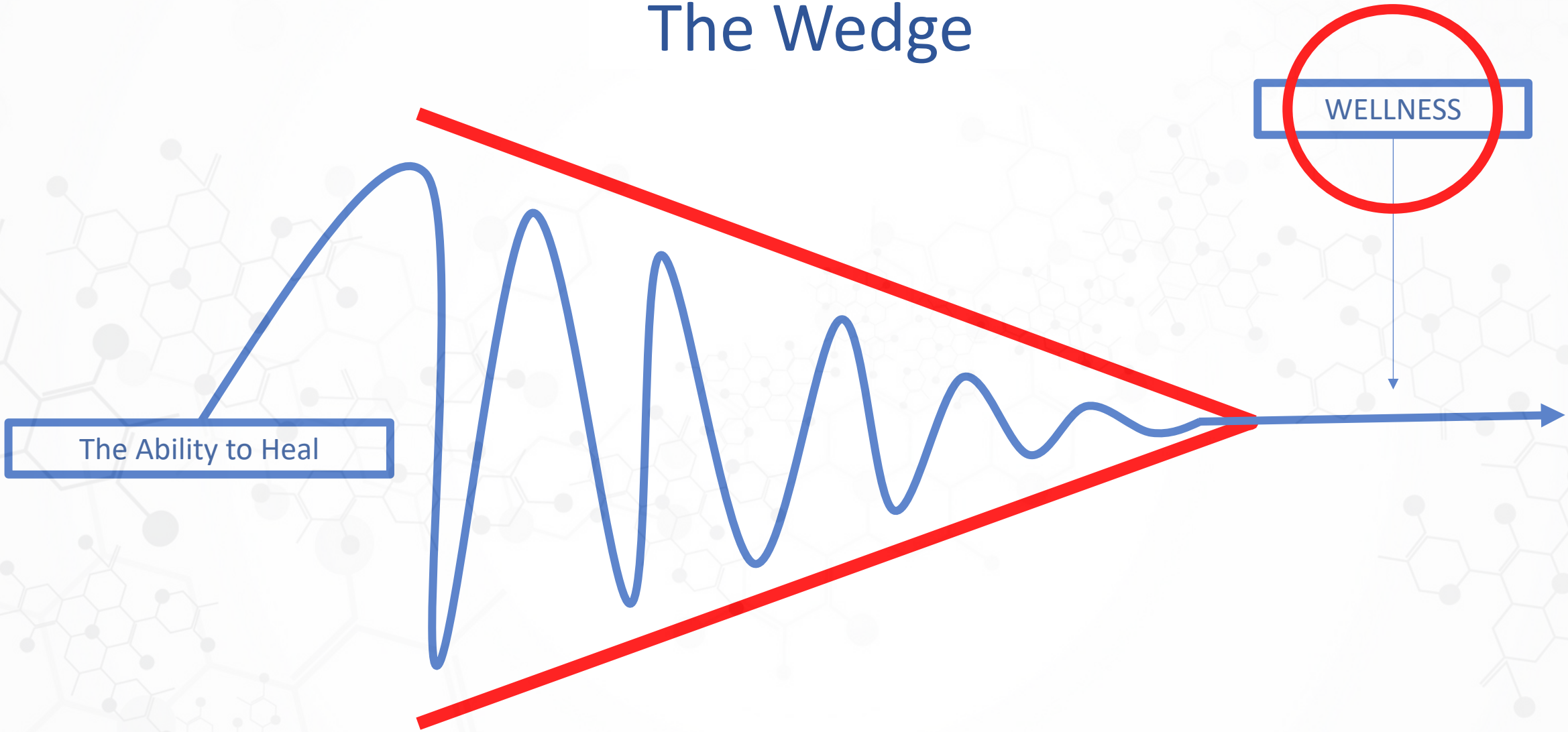
Preservatives

The Wedge



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