Casual Friday Series

Working Through Menopause

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.*

Menopause: What your patients are reading…

Menopause is the time that marks the end of your menstrual cycles. It's diagnosed after you've gone 12 months without a menstrual period. Menopause can happen in your 40s or 50s, but the average age is 51 in the United States.

Menopause is a natural biological process. But the physical symptoms, such as hot flashes, and emotional symptoms of menopause may disrupt your sleep, lower your energy or affect emotional health. There are many effective treatments available, from lifestyle adjustments to hormone therapy.

https://www.mayoclinic.org/diseases-conditions/menopause/symptoms-causes/syc-20353397

Menopause: What your patients are reading…

In the months or years leading up to menopause (perimenopause):

- Irregular periods
- Vaginal dryness
- Hot flashes
- Chills
- Night sweats
- Sleep problems
- Mood changes
- Weight gain and slowed metabolism
- Thinning hair and dry skin
- Loss of breast fullness

https://www.mayoclinic.org/diseases-conditions/menopause/symptoms-causes/syc-20353397

Menopause: What your patients are reading…

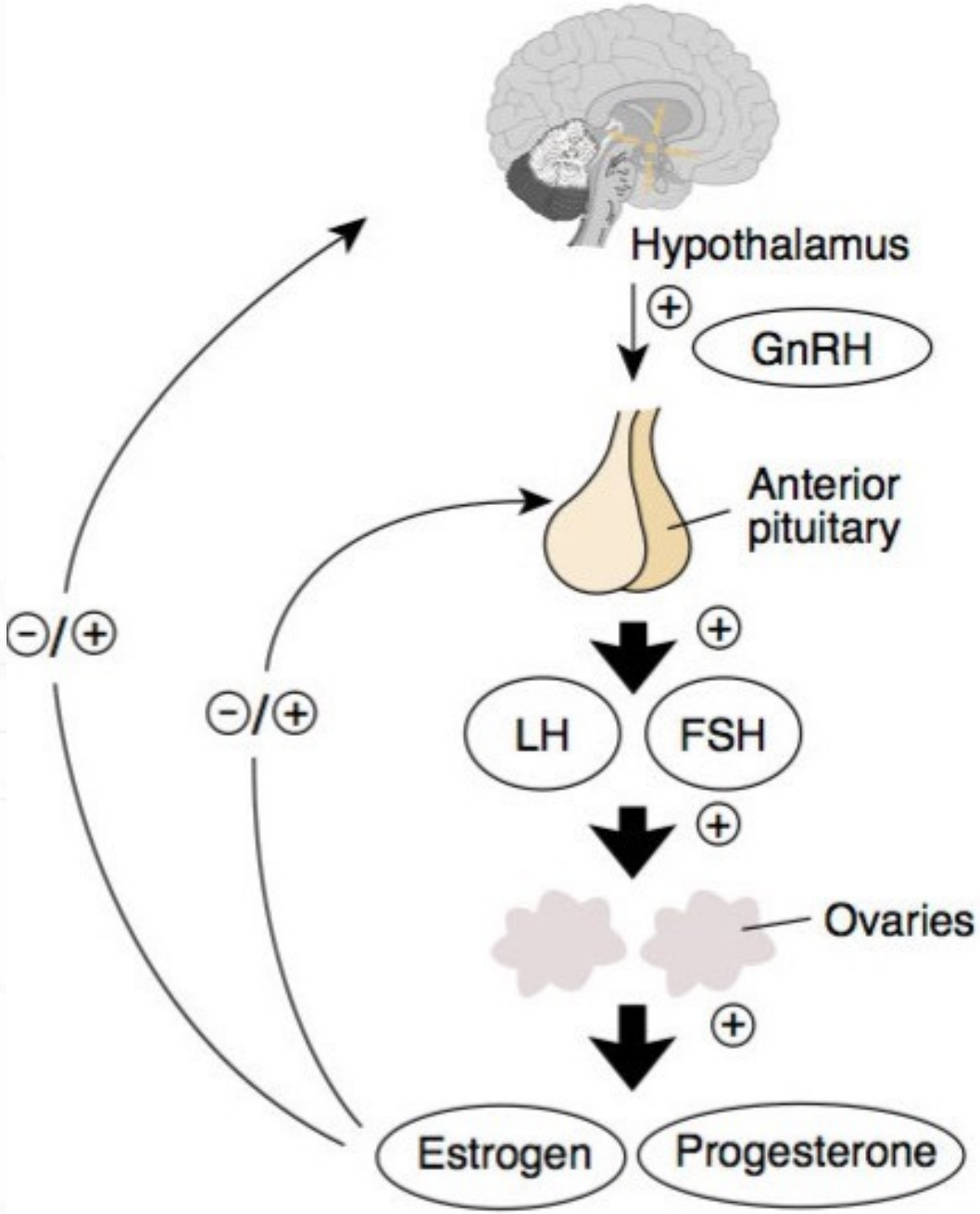
Causes:

1. Naturally declining reproductive hormones
2. Surgery that removes ovaries (oophorectomy)
3. Chemo and radiation therapy
4. Primary ovarian insufficiency

Results:

1. Increased risk for CVD
2. Osteoporosis
3. Bladder function
4. Sexual function
5. Weight gain

https://www.mayoclinic.org/diseases-conditions/menopause/symptoms-causes/syc-20353397



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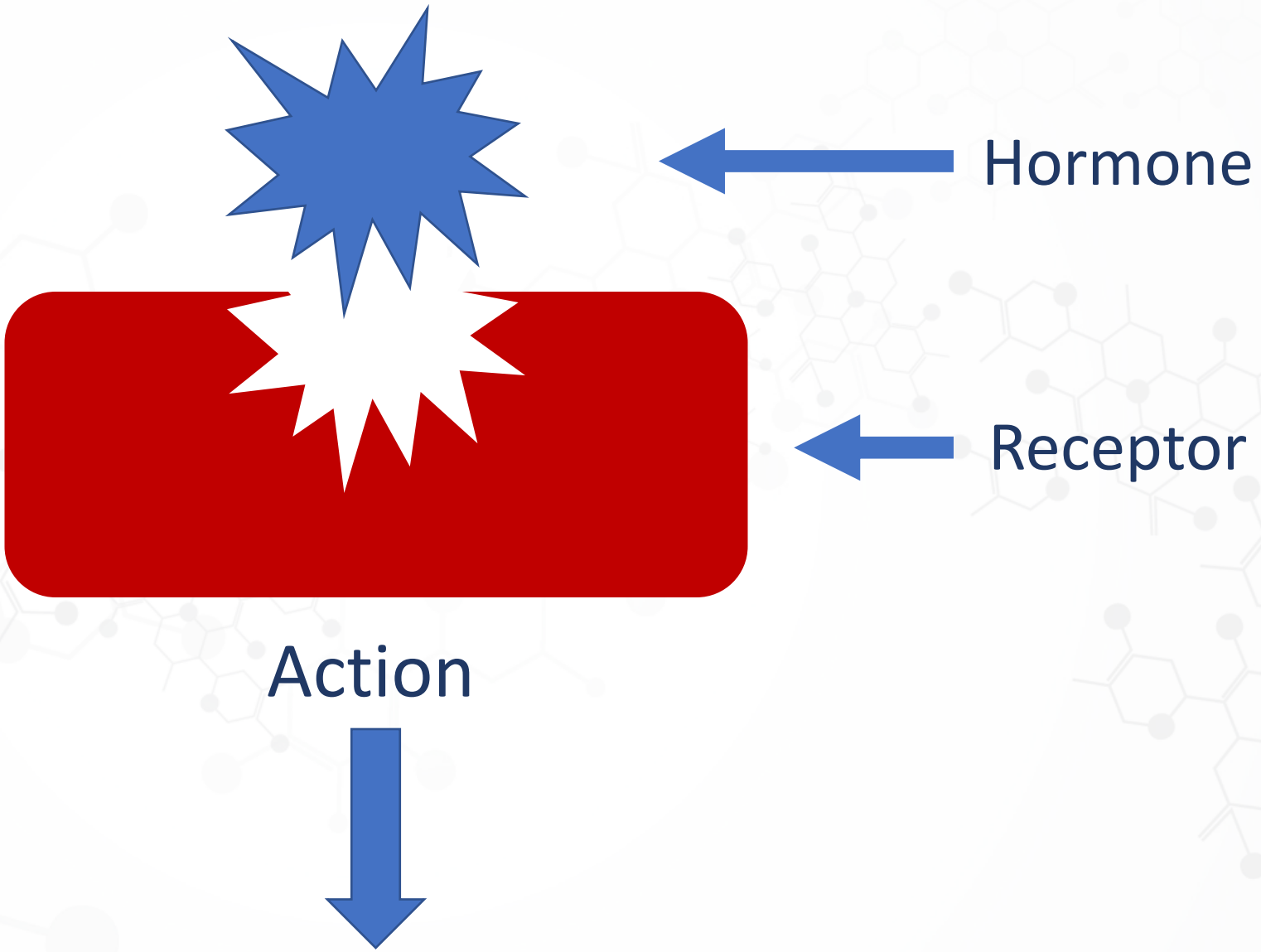
Hormone
Receptor
Action

Minerva Ginecol. Author manuscript; available in PMC 2015 May 2.
PMCID: PMC4417336
Published in final edited form as:
NIHMSID: NIHMS683524
Minerva Ginecol. 2013 Dec; 65(6): 641–651.
PMID: 24346252

Ovarian adrenal interactions during the menopausal transition

R. J. Lasley [1] S. L. Crawford [2] and D. S. Mesenbrink [3]

Observations over the past decade using longitudinal data reveal a gender-specific shift in adrenal steroid production. This shift is represented by an increase in the circulating concentrations of delta 5 steroids in 85% of all women and is initiated only after the menopausal transition has begun. While the associated rise in the major adrenal androgen, dehydroepiandrosterone sulfate (DHEAS), is modest, the parallel rises in dehydroepiandrosteone (DHEA) and androstenediol (Adiol) are much more robust. These increases in circulating steroid concentrations are qualitatively similar on average between ethnicities but quantitatively different between individual women. Both circulating testosterone (T) and androstenedione (Adione) also rise concomitantly but modestly by comparison. This phenomenon presents a new and provocative aspect to the endocrine foundations of the menopausal transition and may provide important clues to understanding the fundamentals of mid-aged women's healthy aging, particularly an explanation for the wide diversity in phenotypes observed during the MT as well as their different responses to hormone replacement therapies. Experimental studies using the nonhuman primate animal model show an acute adrenal response to human chorionic gonadotropin (hCG) challenge as well as the presence of luteinizing hormone receptors (LHR) in their adrenal cortices. These experimental results support the concept that LHRs are recruited to the adrenal cortices of mid-aged women that subsequently function to respond to increasing circulating LH to shunt pregnenolone metabolites towards the delta 5 pathway. Future investigations are required to determine the relationship of these changes in adrenal function to symptoms and health outcomes of mid-aged women.

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PMCID: PMC3366061

NIHMSID: NIHMS339770

PMID: 22415563

Androstenediol Complements Estrogenic Bioactivity during the Menopausal Transition

Bill L. Lasley, Ph.D.,[1] Jiangang Chen, Ph.D.,[1] Frank Z. Stanczyk, Ph.D.,[2] Samar R. El Khoudary, Ph.D., M.P.H,[3] Nancy A Gee, B.S.,[1] Sybil Crawford, Ph.D.,[4] and Daniel S. McConnell, Ph.D.[5,*]

A two-fold increase in circulating Adione and T was found to rise in parallel with the rise in circulating DHEAS, while DHEA and Adiol concentrations rose seven to eightfold. Circulating Adiol, which has both androgenic and estrogenic biological activity, was significantly associated ($p<0.02$) with circulating estrogen bioactivity only when E2 concentrations were low and Adiol levels were high.

The wide range of circulating levels of Adiol and its contribution to total circulating estrogenicity during the MT is consistent with the observed inter-woman difference in symptoms at this time. Therefore, we conclude that Adiol contributes to circulating estrogenicity when E2 production falls at menopause and may contribute significantly to the endocrine changes experienced by midlife women.

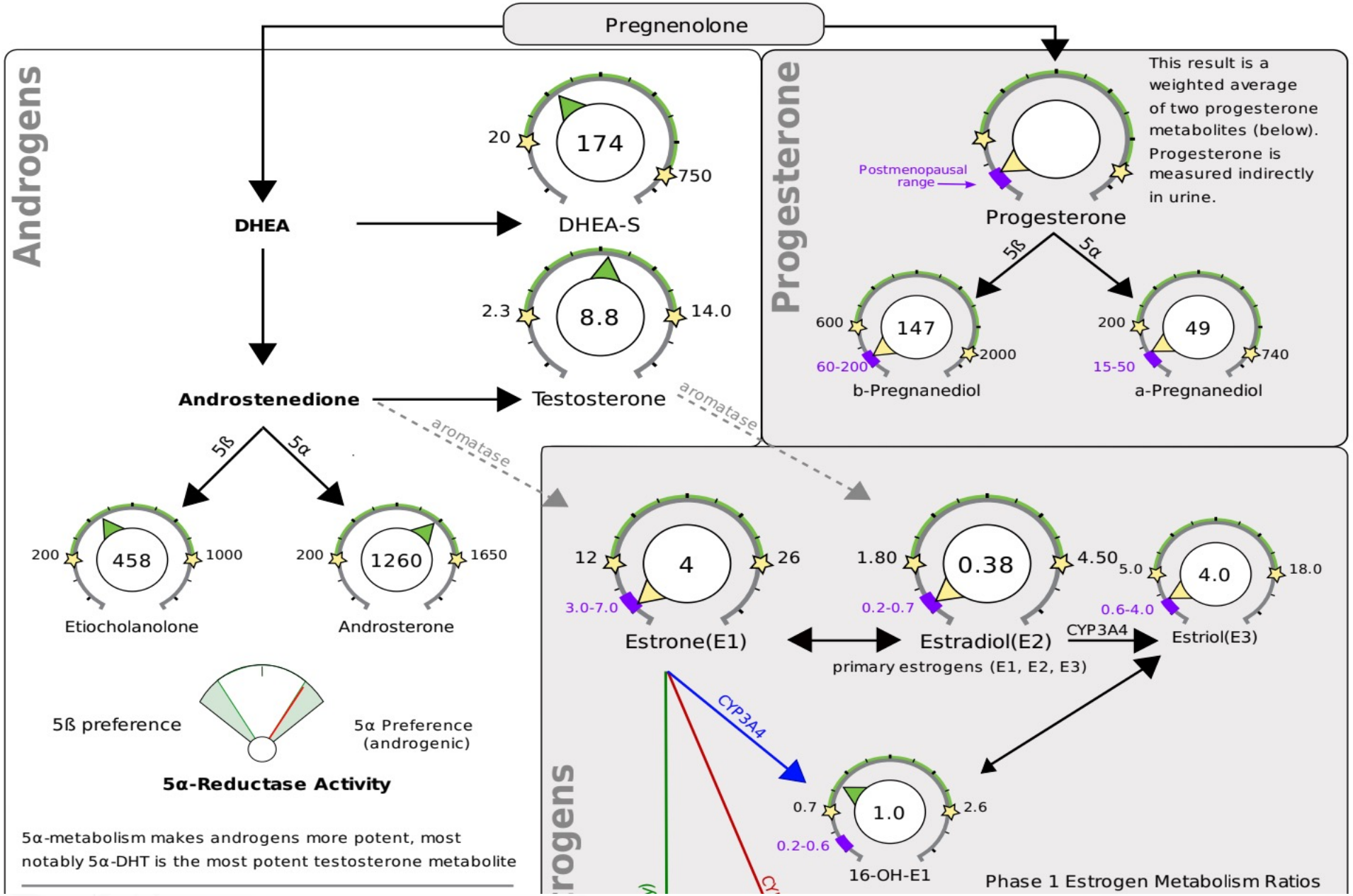
Other Hormones and Their Roles

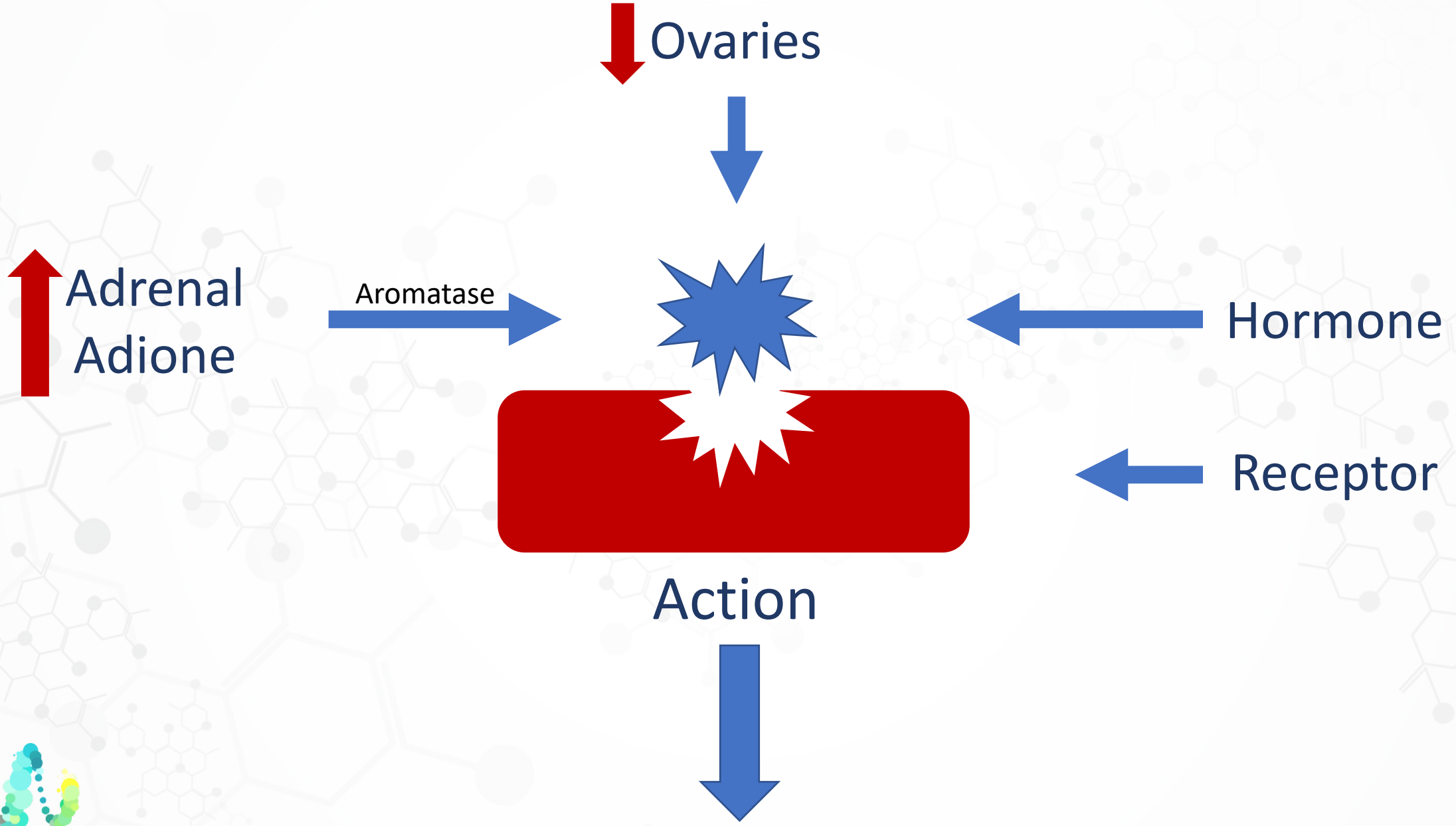
Peter C. Hindmarsh, Kathy Geertsma, in Congenital Adrenal Hyperplasia, 2017

Androstenedione

Androstenedione is made in the adrenal glands as well as the testes and ovaries. In females, androstenedione is converted to provide around half of all testosterone and almost all of the body's estrone, a form of estrogen. Although the testes produce large amounts of androstenedione in males, they secrete little of this into the blood and instead, rapidly convert it into testosterone within the testes. The

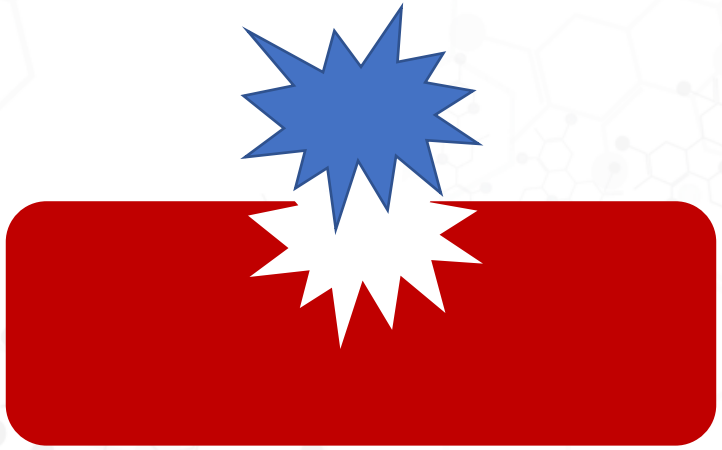
https://www.sciencedirect.com/topics/medicine-and-dentistry/androstenedione


Pregnenolone
Androgens
DHEA
20
174
750
DHEA-S
2.3
8.8
14.0
Androstenedione
Testosterone
aromatase
aromatase
5ß
5α
200
458
1000
Etiocholanolone
200
1260
1650
Androsterone
5ß preference
5α Preference
(androgenic)
5α-Reductase Activity
5α-metabolism makes androgens more potent, most notably 5α-DHT is the most potent testosterone metabolite
Progesterone
This result is a weighted average of two progesterone metabolites (below). Progesterone is measured indirectly in urine.
Postmenopausal range
Progesterone
5ß
5α
600
147
2000
60-200
b-Pregnanediol
200
49
740
15-50
a-Pregnanediol
12
4
26
3.0-7.0
Estrone(E1)
1.80
0.38
4.50
0.2-0.7
Estradiol(E2)
CYP3A4
5.0
4.0
18.0
0.6-4.0
Estriol(E3)
primary estrogens (E1, E2, E3)
CYP3A4
0.7
1.0
2.6
0.2-0.6
16-OH-E1
Phase 1 Estrogen Metabolism Ratios

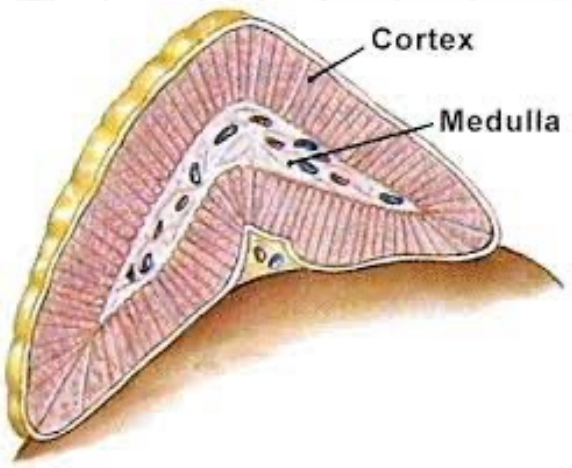

Ovaries
Adrenal
Adione
Aromatase
Hormone
Receptor
Action

3 Options for intervention:

replace

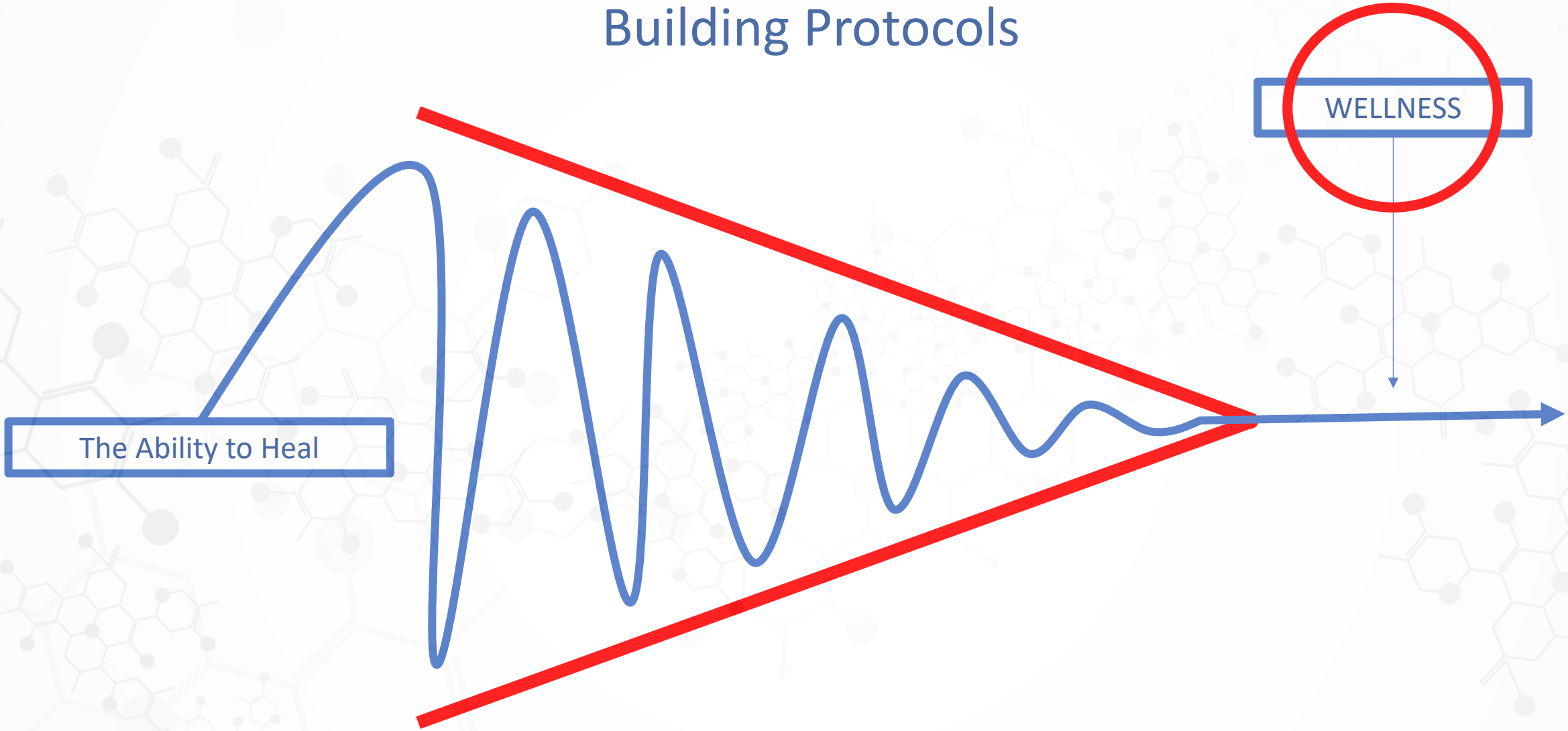


sensitize

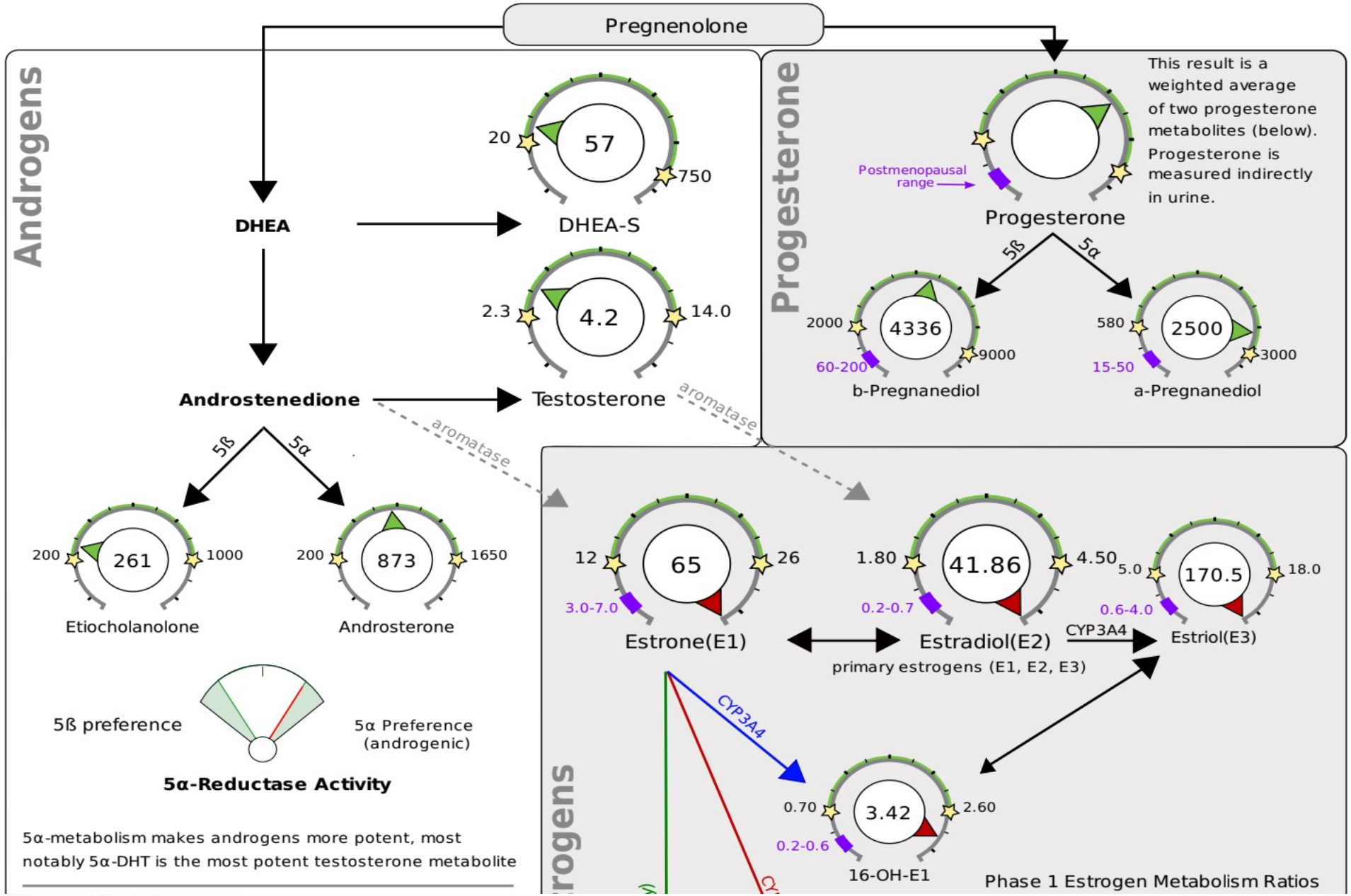


support

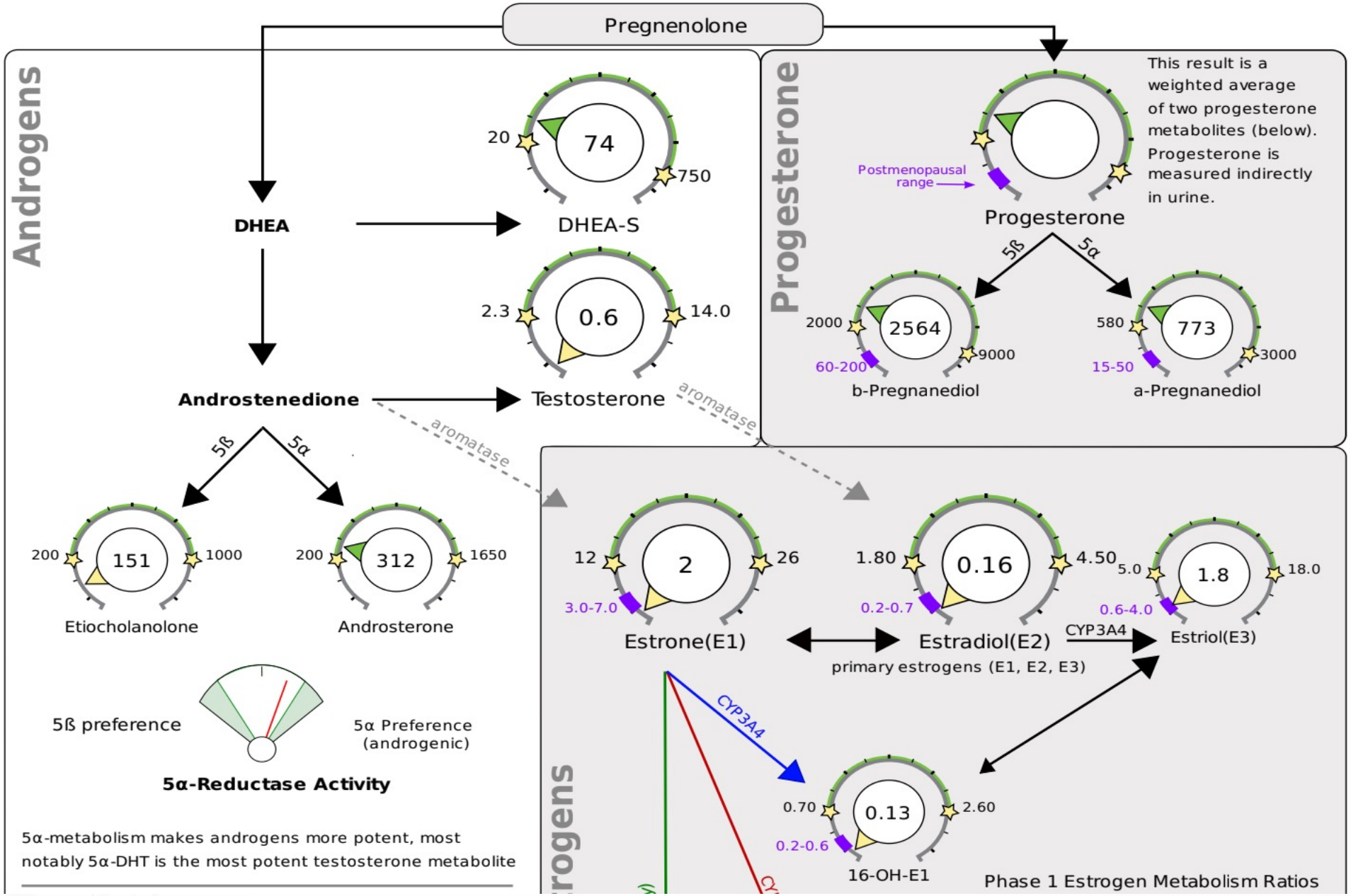
Building Protocols



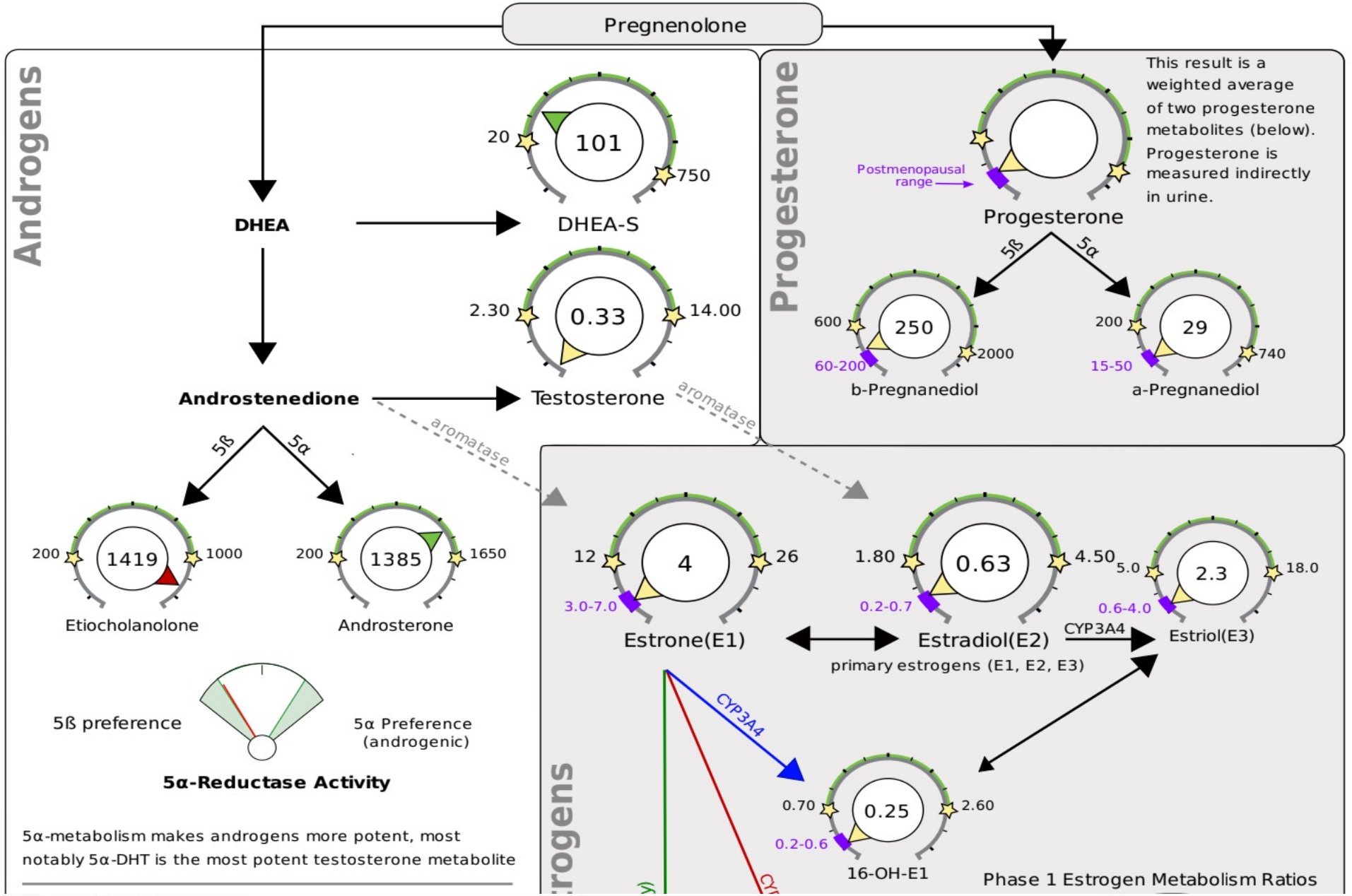
1


Pregnenolone
Androgens
DHEA
20
57
750
DHEA-S
2.3
4.2
14.0
Androstenedione
Testosterone
aromatase
aromatase
5ß
5α
200
261
1000
Etiocholanolone
200
873
1650
Androsterone
5ß preference
5α Preference (androgenic)
5α-Reductase Activity
5α-metabolism makes androgens more potent, most notably 5α-DHT is the most potent testosterone metabolite
Progesterone
This result is a weighted average of two progesterone metabolites (below). Progesterone is measured indirectly in urine.
Postmenopausal range
Progesterone
5ß
5α
2000
4336
9000
60-200
b-Pregnanediol
580
2500
3000
15-50
a-Pregnanediol
12
65
26
3.0-7.0
Estrone(E1)
1.80
41.86
4.50
0.2-0.7
Estradiol(E2)
CYP3A4
5.0
170.5
18.0
0.6-4.0
Estriol(E3)
primary estrogens (E1, E2, E3)
CYP3A4
0.70
3.42
2.60
0.2-0.6
16-OH-E1
Phase 1 Estrogen Metabolism Ratios

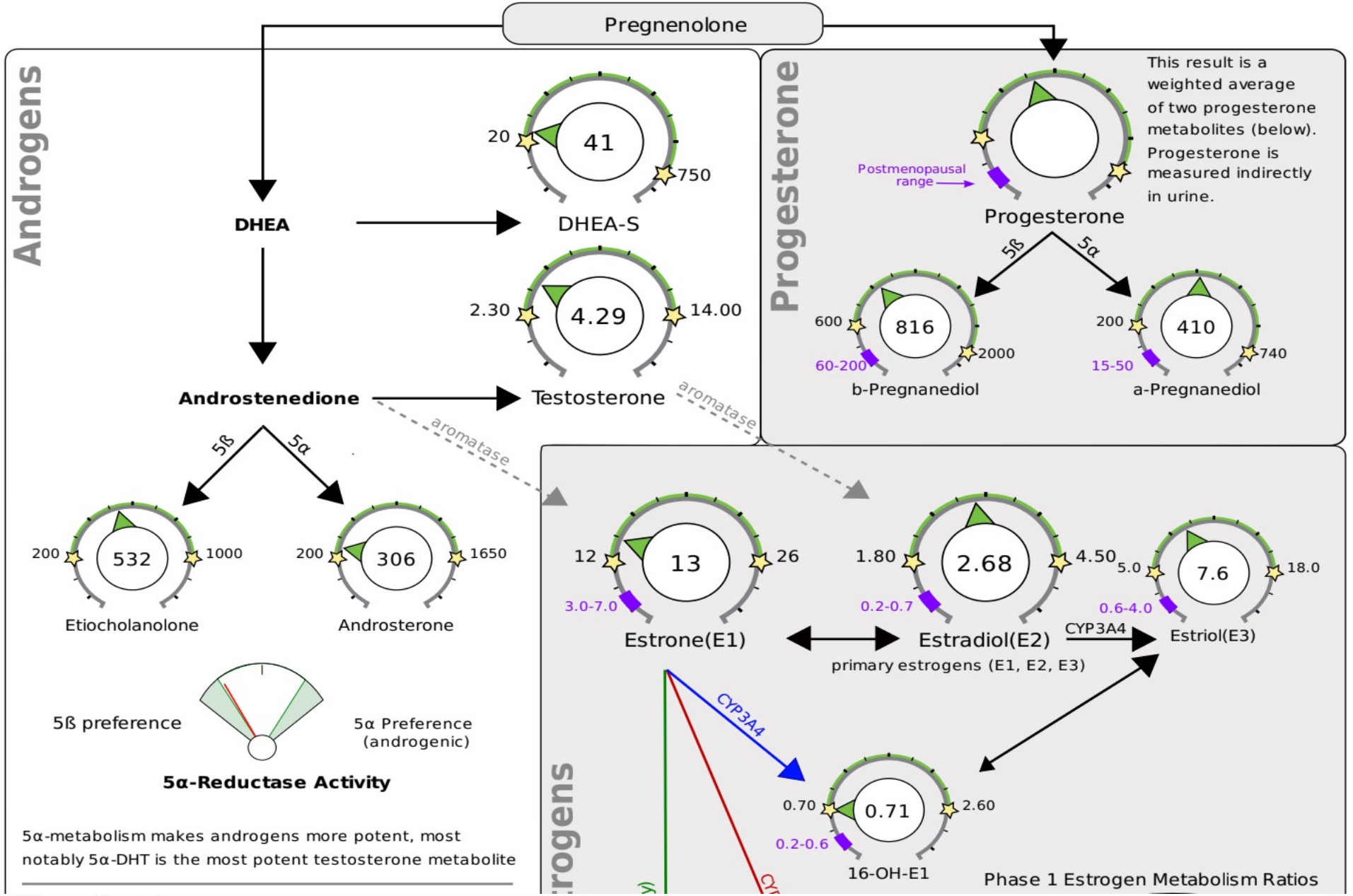
2


Pregnenolone
Androgens
DHEA
20
74
750
DHEA-S
2.3
0.6
14.0
Androstenedione
Testosterone
aromatase
aromatase
5ß
5α
200
151
1000
Etiocholanolone
200
312
1650
Androsterone
5ß preference
5α Preference
(androgenic)
5α-Reductase Activity
5α-metabolism makes androgens more potent, most notably 5α-DHT is the most potent testosterone metabolite
Progesterone
This result is a weighted average of two progesterone metabolites (below). Progesterone is measured indirectly in urine.
Postmenopausal range
Progesterone
5ß
5α
2000
2564
9000
60-200
b-Pregnanediol
580
773
3000
15-50
a-Pregnanediol
12
2
26
3.0-7.0
Estrone(E1)
1.80
0.16
4.50
0.2-0.7
Estradiol(E2)
CYP3A4
5.0
1.8
18.0
0.6-4.0
Estriol(E3)
primary estrogens (E1, E2, E3)
CYP3A4
0.70
0.13
2.60
0.2-0.6
16-OH-E1
Phase 1 Estrogen Metabolism Ratios

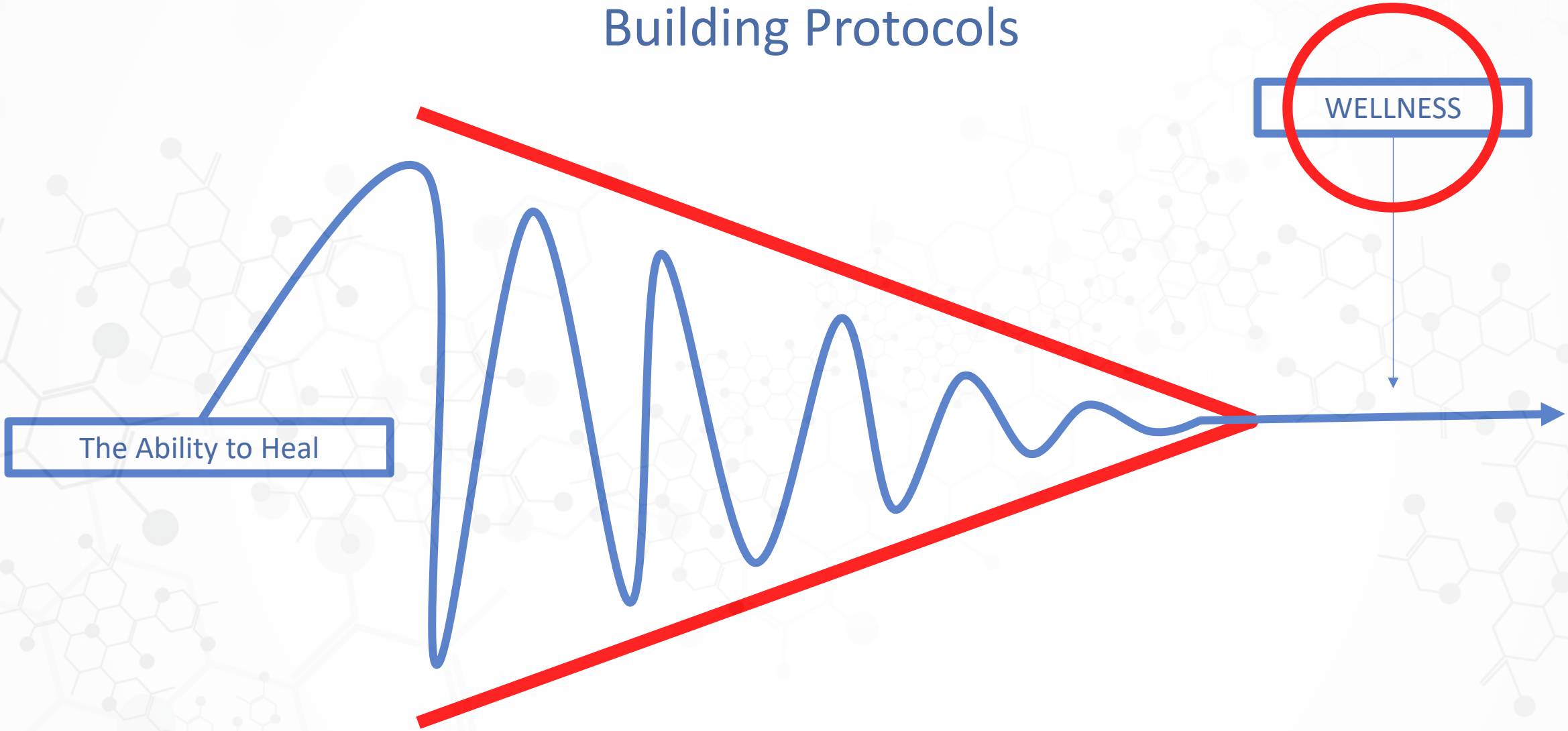
3


Pregnenolone
Androgens
DHEA
20
101
750
DHEA-S
2.30
0.33
14.00
Androstenedione
Testosterone
aromatase
aromatase
5ß
5α
200
1419
1000
Etiocholanolone
200
1385
1650
Androsterone
5ß preference
5α Preference
(androgenic)
5α-Reductase Activity
5α-metabolism makes androgens more potent, most notably 5α-DHT is the most potent testosterone metabolite
Progesterone
This result is a weighted average of two progesterone metabolites (below). Progesterone is measured indirectly in urine.
Postmenopausal range
Progesterone
5ß
5α
600
250
2000
60-200
b-Pregnanediol
200
29
740
15-50
a-Pregnanediol
12
4
26
3.0-7.0
Estrone(E1)
1.80
0.63
4.50
0.2-0.7
Estradiol(E2)
CYP3A4
5.0
2.3
18.0
0.6-4.0
Estriol(E3)
primary estrogens (E1, E2, E3)
CYP3A4
0.70
0.25
2.60
0.2-0.6
16-OH-E1
Phase 1 Estrogen Metabolism Ratios

4


Pregnenolone
Androgens
DHEA
20
41
750
DHEA-S
2.30
4.29
14.00
Androstenedione
Testosterone
aromatase
aromatase
5ß
5α
200
532
1000
Etiocholanolone
200
306
1650
Androsterone
5ß preference
5α Preference
(androgenic)
5α-Reductase Activity
5α-metabolism makes androgens more potent, most notably 5α-DHT is the most potent testosterone metabolite
Progesterone
This result is a weighted average of two progesterone metabolites (below). Progesterone is measured indirectly in urine.
Postmenopausal range
Progesterone
5ß
5α
600
816
2000
60-200
b-Pregnanediol
200
410
740
15-50
a-Pregnanediol
12
13
26
3.0-7.0
Estrone(E1)
1.80
2.68
4.50
0.2-0.7
Estradiol(E2)
CYP3A4
5.0
7.6
18.0
0.6-4.0
Estriol(E3)
primary estrogens (E1, E2, E3)
CYP3A4
0.70
0.71
2.60
0.2-0.6
16-OH-E1
Phase 1 Estrogen Metabolism Ratios

Building Protocols



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