Casual Friday Series

Female HRT and Chronic Disease

A Biogenetix Clinical Presentation

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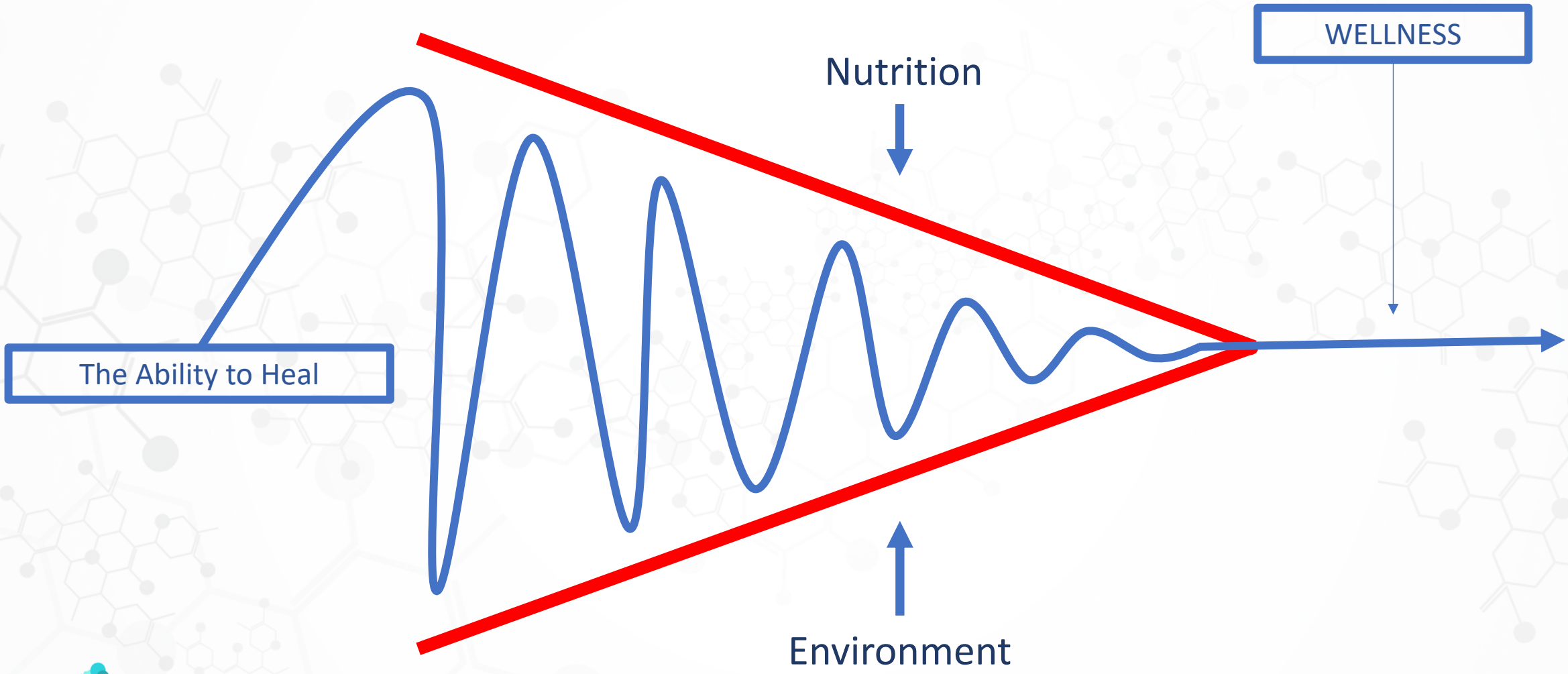
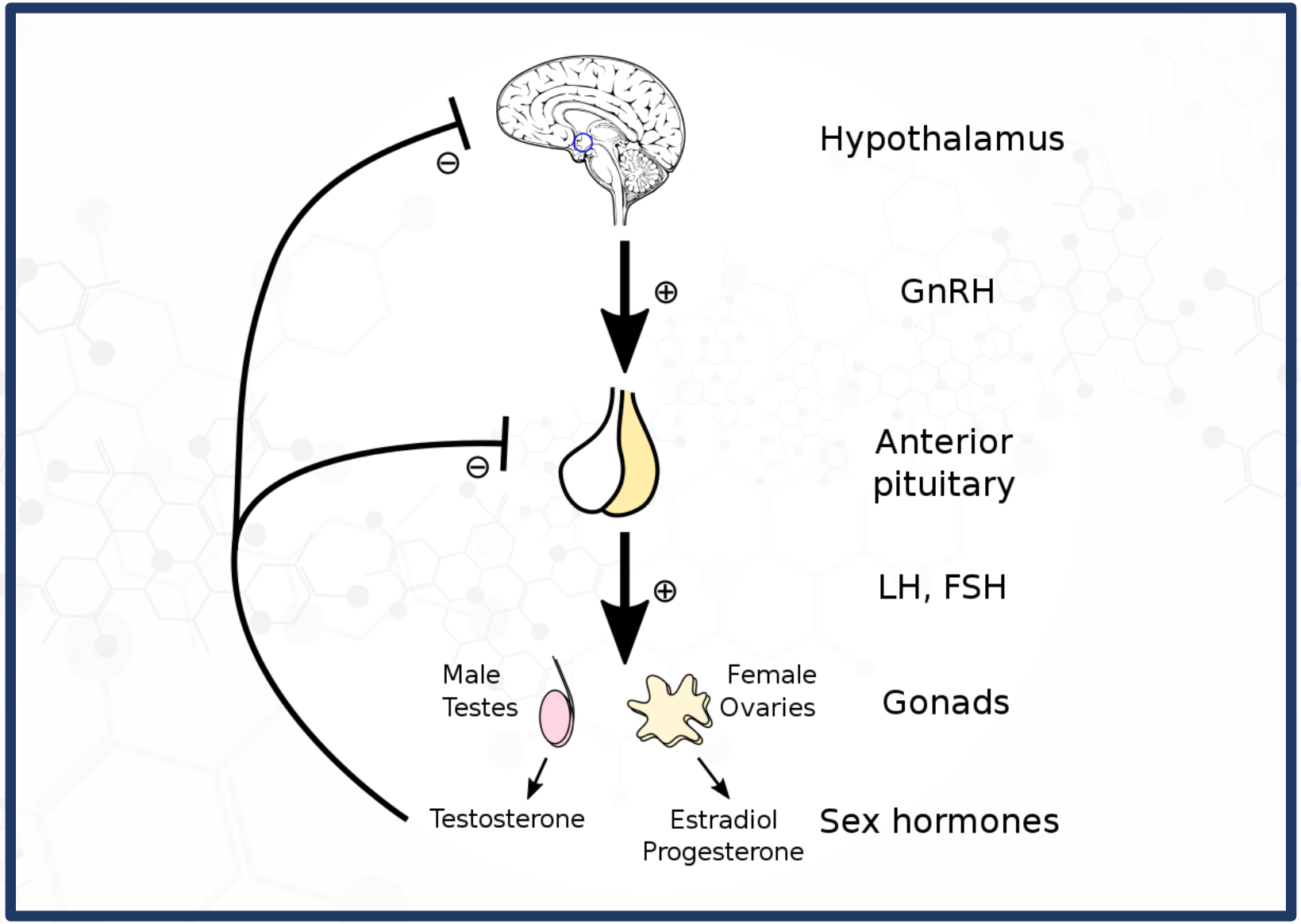
Disclaimer

- *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.*

Lifestyle + Genetics = Chronic Health IMPROVEMENT

Protocols





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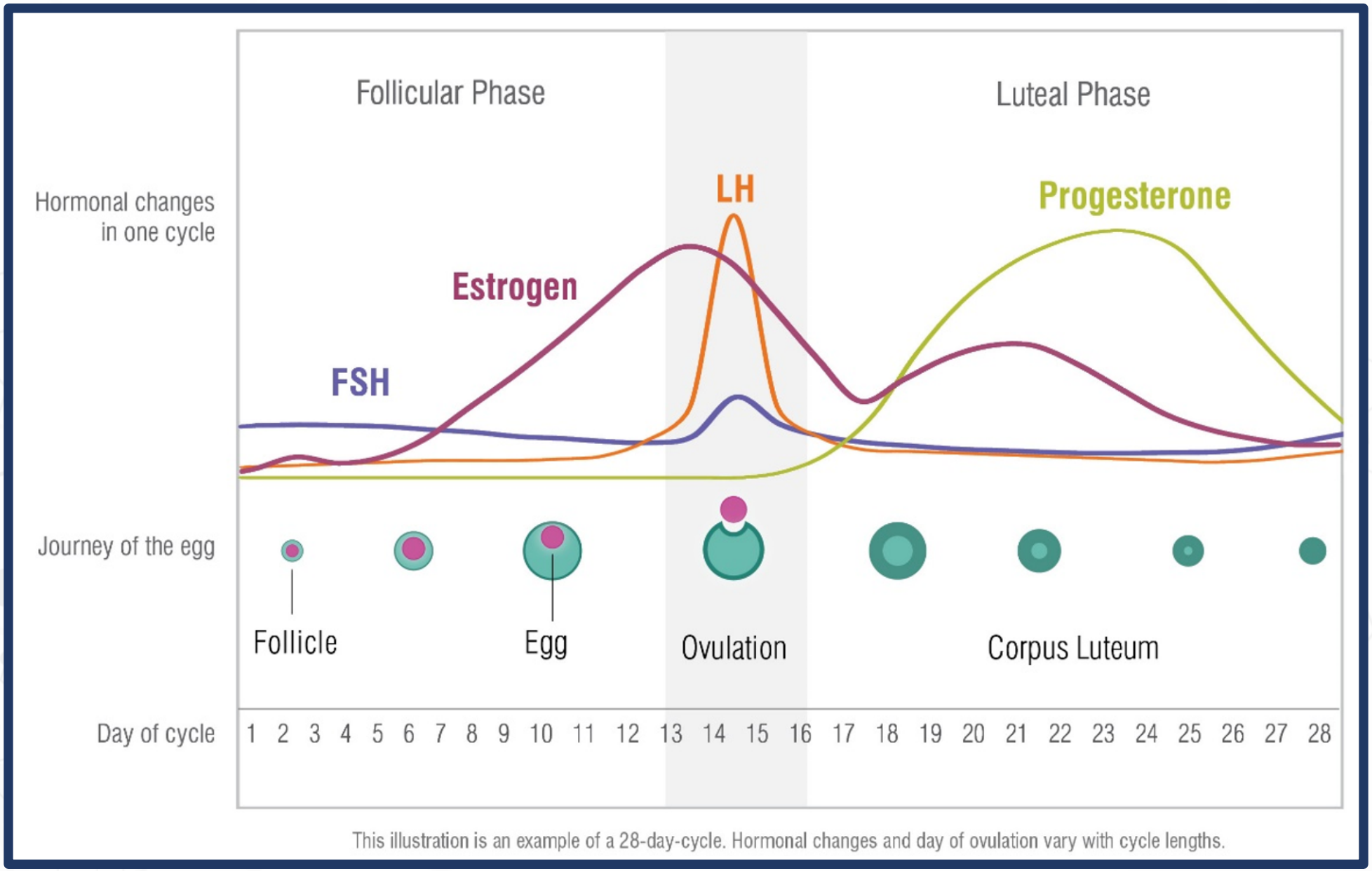
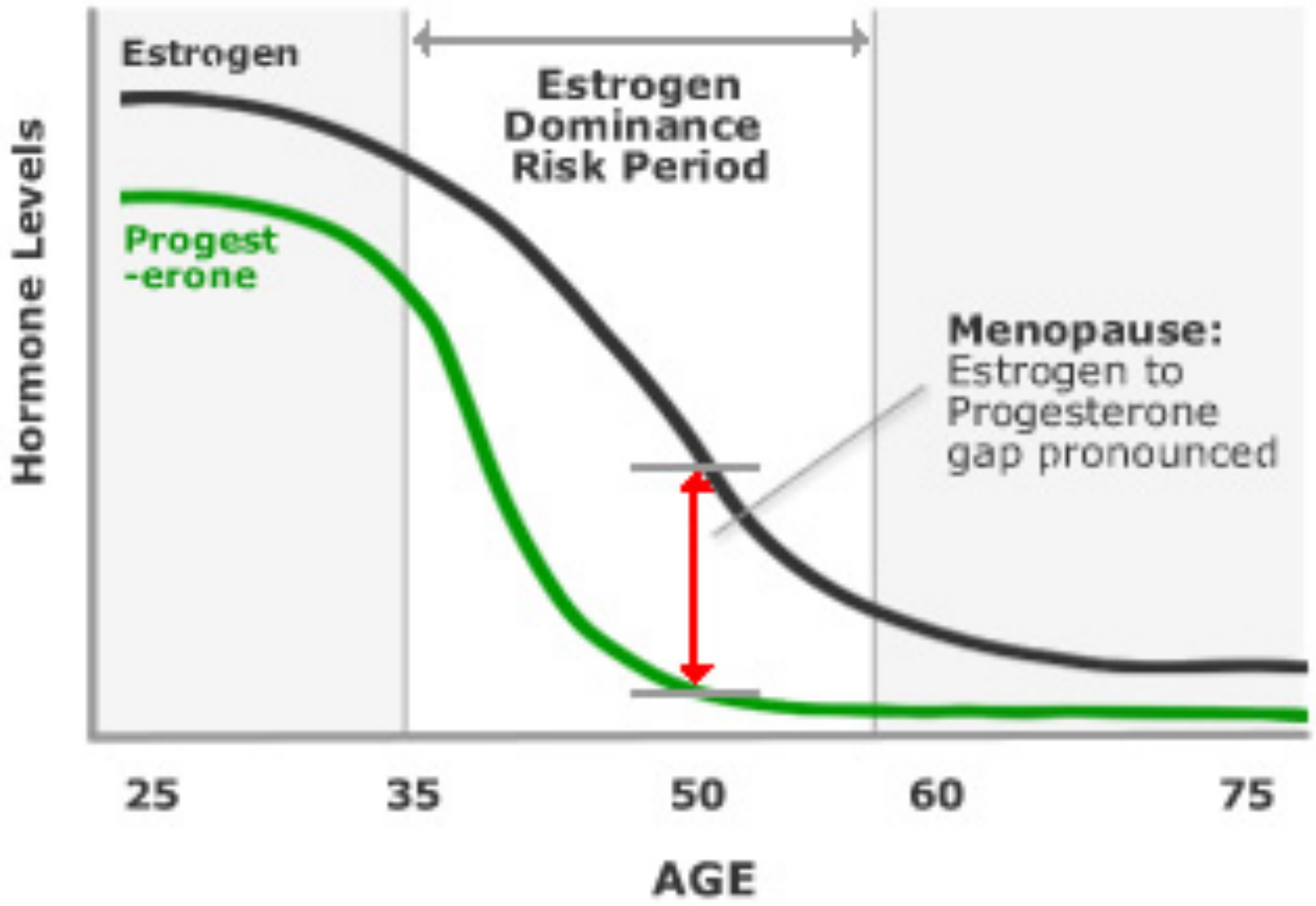


https://www.zrtlab.com/media/2509/how-your-hormones-affect-athletic-performance-and-why-you-need-to-start-testing-image.png



https://rootedinhealth.ca/wp-content/uploads/2015/09/Estrogen-dominance-menopause-graph.jpg

Review > J Epidemiol Biostat. 1999;4(3):191-210; discussion 210-5.

Use of HRT and the subsequent risk of cancer

At least 20 million women in developed countries are estimated to be currently using hormone replacement therapy (HRT). Almost 100 epidemiological studies have reported on the relationship between the use of HRT and the risk of cancer of female reproductive organs, namely the breast, uterus or ovary. Cancer at these sites is common and there are a priori reasons why the use of hormonal therapy to 'replace' the endogenous production of ovarian hormones after the menopause might increase the risk of these cancers. The available evidence indicates that the risk of breast cancer or endometrial cancer is increased while women are using HRT, the risk increasing with increasing duration of use. Most of the evidence about these cancers relates to use of HRT preparations containing oestrogens alone. The limited evidence about combination therapy, with oestrogens and progestogens, suggests that, compared to oestrogens alone, the effect on the breast is similar, but the effect on the endometrium is diminished, the diminution in risk being greater the more days each month that progestogens are used. The effect of HRT on breast cancer wears off after use ceases and

Review > J Epidemiol Biostat. 1999;4(3):191-210; discussion 210-5.

Use of HRT and the subsequent risk of cancer

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month that progestogens are used. The effect of HRT on breast cancer wears off after use ceases and has disappeared largely, if not wholly, within 5 years, whereas the effects on endometrial cancer take longer to wear off, if at all. The breast and endometrial cancers that are diagnosed in HRT users are less aggressive clinically than cancers in never-users but, as yet, there is little reliable information about the relationship between use of HRT and mortality from these cancers. For other cancer sites, the existing data about the effects of HRT are inconclusive. The longer the period of use of HRT, the greater the excess incidence of cancer of the breast and endometrium is likely to be. Use of HRT for short periods of time should have little effect on the incidence of these cancers. The cumulative excess incidence in 1000 women who used HRT for 10 years, beginning at age 50, is estimated to be six for breast cancer, 42 for endometrial cancer in women with an intact uterus using oestrogen therapy alone and about 20 for endometrial cancer in women with an intact uterus using oestrogen-progestogen combinations. The estimate for combined therapy is based on small numbers and may well vary with the type of preparation used. The overall balance between the excess incidence of these cancers and other effects of HRT needs to be evaluated carefully and will require more reliable data than exist at present.

Review > Steroids. 2015 Jul;99(Pt A):56-60. doi: 10.1016/j.steroids.2014.08.006.
Epub 2014 Aug 24.

Mechanisms of estrogen carcinogenesis: The role of E2/E1-quinone metabolites suggests new approaches to preventive intervention--A review

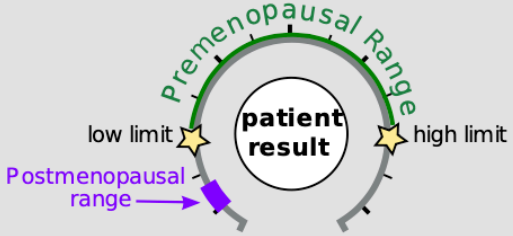
James D Yager [1]

carcinogenic in the kidney, uterus and mammary gland. Observational studies and clinical trials consistently show that sustained exposure to E2/E1 is associated with the development of sporadic breast cancer. The weight of evidence supports the contribution of two complementary pathways in the initiation, promotion and progression of breast cancer. One pathway involves activation of nuclear and cytoplasmic signaling pathways through the binding of estrogen to nuclear and membrane-bound estrogen receptors leading to increased cell proliferation. The other pathway involves the oxidative metabolism of E2/E1 to catechols and then reactive quinones that can contribute to oxidative DNA damage and form specific, mutagenic depurinating adducts with adenine and guanine which then in turn can serve as biomarkers for the occurrence of these processes. Both pathways

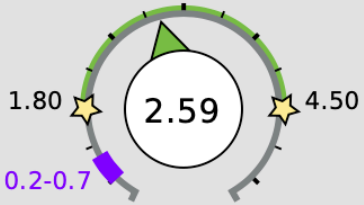
50 y.o. female, hypothyroid and pre-DM

Hormone Testing Summary

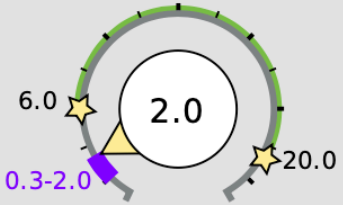
Key (how to read the results):



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



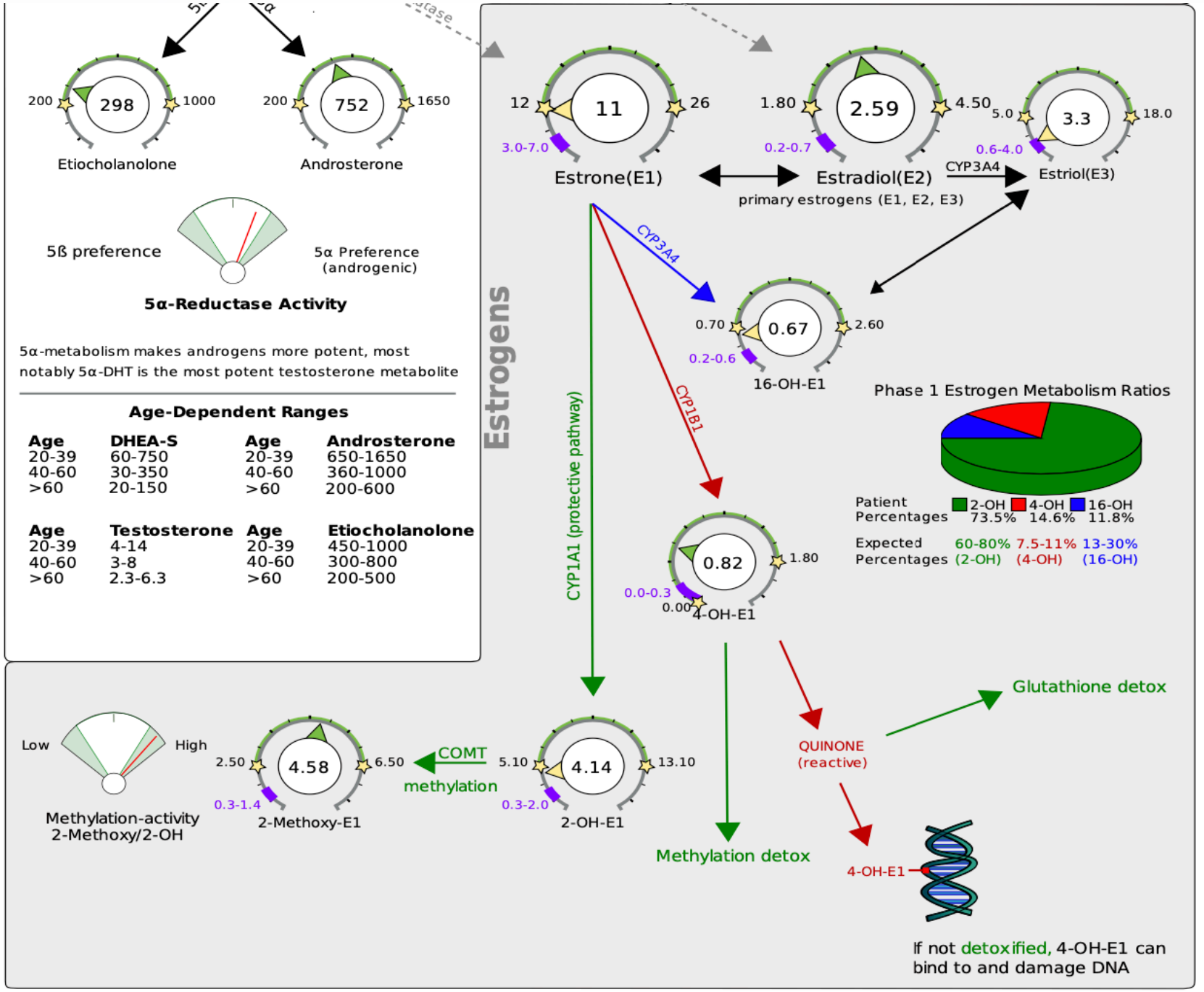
Estradiol(E2)



Progesterone
(Serum Equivalent, ng/mL)

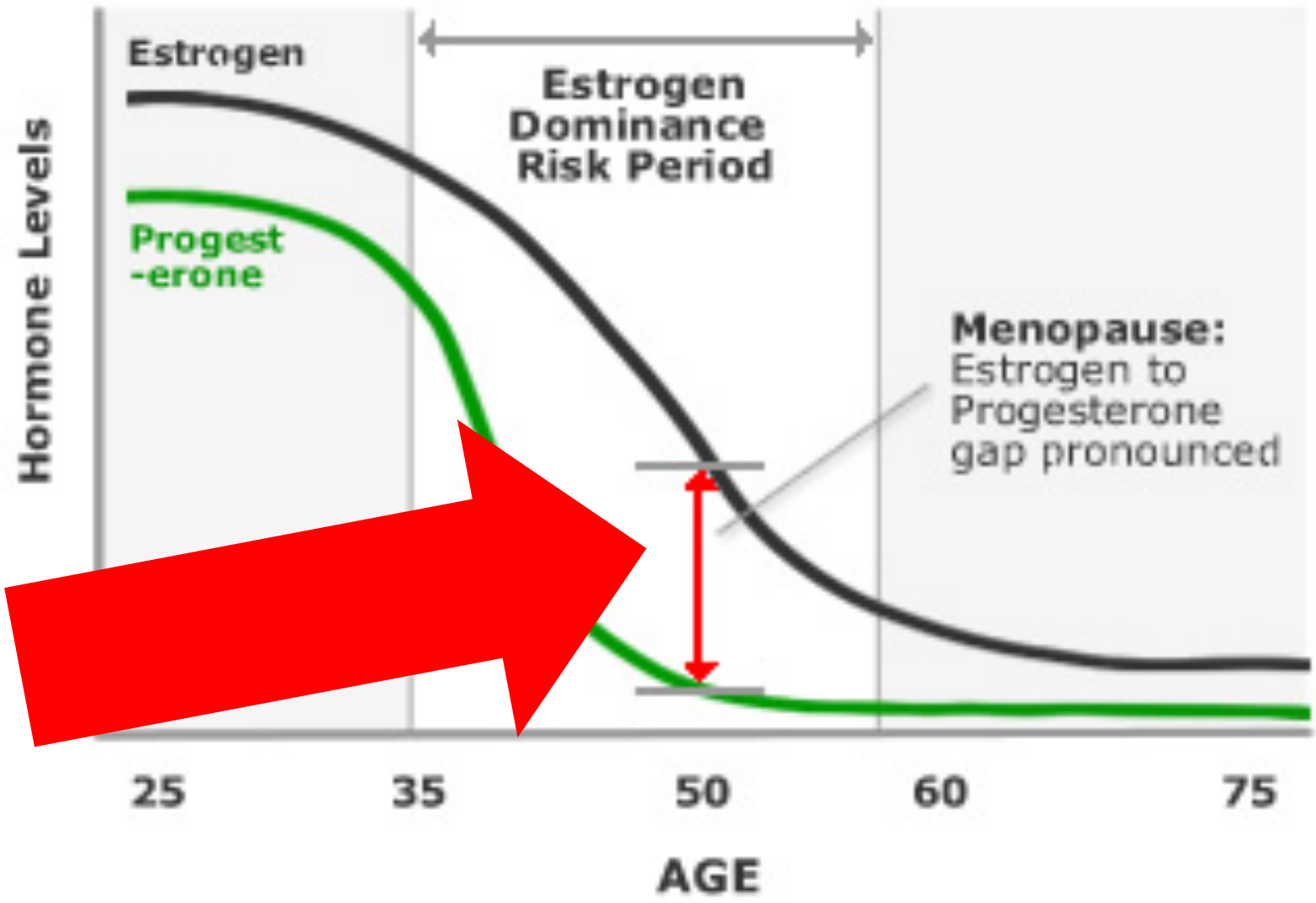
Progesterone Serum Equivalent is a calculated value based on urine pregnanediol.

Testosterone


200
298
1000
Etiocholanolone
200
752
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
Age-Dependent Ranges
Age DHEA-S
20-39 60-750
40-60 30-350
>60 20-150
Age Androsterone
20-39 650-1650
40-60 360-1000
>60 200-600
Age Testosterone
20-39 4-14
40-60 3-8
>60 2.3-6.3
Age Etiocholanolone
20-39 450-1000
40-60 300-800
>60 200-500
12
11
26
3.0-7.0
Estrone(E1)
1.80
2.59
4.50
0.2-0.7
Estradiol(E2)
CYP3A4
5.0
3.3
18.0
0.6-4.0
Estriol(E3)
primary estrogens (E1, E2, E3)
Estrogens
CYP3A4
0.70
0.67
2.60
0.2-0.6
16-OH-E1
CYP1B1
CYP1A1 (protective pathway)
Phase 1 Estrogen Metabolism Ratios
Patient Percentages
2-OH 73.5%
4-OH 14.6%
16-OH 11.8%
Expected Percentages
60-80% (2-OH)
7.5-11% (4-OH)
13-30% (16-OH)
0.82
1.80
0.0-0.3
0.00
4-OH-E1
Glutathione detox
QUINONE (reactive)
Low
High
Methylation-activity
2-Methoxy/2-OH
2.50
4.58
6.50
0.3-1.4
2-Methoxy-E1
COMT
methylation
5.10
4.14
13.10
0.3-2.0
2-OH-E1
Methylation detox
4-OH-E1
If not detoxified, 4-OH-E1 can bind to and damage DNA

The Perfect Storm

1. 45-65 years old
2. Estrogen dominant
3. Gallbladder has been removed
4. Low fat diet
5. Genetically favors her 4–0H detox pathway
6. Unaccounted for / contributing factors:
    - Alcohol use
    - Environmental exposures
    - Dietary exposure of foreign chemicals
    - Carbohydrate intake



https://rootedinhealth.ca/wp-content/uploads/2015/09/Estrogen-dominance-menopause-graph.jpg

Table 1 Systemic HRT Treatment Options

Treatment	Dosage	Evidence of Benefit	FDA Approval	Products[a]
Conjugated estrogens	Standard: 0.625 mg/day Low: 0.3-0.45 mg/day	Yes	Yes Yes	Premarin (tablet or injectable) Prempro, Premphase (CEE/medroxyprogesterone)
Micronized 17β estradiol	Standard: 1 mg/day Low: 0.5 mg/day Ultralow: 0.25 mg/day	Yes Yes Mixed	Yes Yes No	Estrace (tablet) Estradiol tablets (generic) Menest (esterified estrogens)
Transdermal 17β estradiol	Standard: 0.0375-0.05 mg/day Low: 0.025 mg/day Ultralow: 0.014 mg/day	Yes Yes Mixed	Yes Yes No	Alora (twice weekly) Climara (weekly) Divigel (0.1% estradiol gel) Elestrin (0.06% estradiol gel) Estrasorb (4.35 mg/1.74 g emulsion) Estrogel (0.06% estradiol gel) EvaMist (spray) Menostar (weekly) Minivelle (twice weekly) Vivelle-Dot (twice weekly)
Estradiol acetate ring	0.05 mg/day	Yes	Yes	Femring 0.05 mg or 0.1 mg estradiol daily over 3 mo (no substitutes)
Conjugated estrogens with bazedoxifene	0.45 mg/20 mg daily	Yes	Yes	Duavee (CEE/bazedoxefine)
Combination estrogen-progestin	Various	Yes	Yes	Climara Pro (estradiol/levonorgestrel weekly patch) Combipatch (estradiol/norethindrone acetate twice-weekly patch) Xulane (ethinyl estradiol/norgestromin patch) Activella (estradiol/norethindrone acetate tablet) Lopreeza (estradiol/norethindrone acetate tablet) Mimvey (estradiol/norethindrone acetate tablet) Femhrt (ethinyl estradiol/norethindrone acetate tablet) Angeliq (estradiol/drosperinone tablet)
Depot progestin	Individualized, injected q3mo	Yes	No	Depo-Provera (medroxyprogesterone acetate)
IM estrogen	Individualized: Cypionate: 1-5 mg IM q3-4w Valerate: 10-20 mg IM q4w		Yes	Delestrogen (estradiol valerate) Depo-Estradiol (estradiol cypionate)

[a] *Many HRT products are not interchangeable. Check interchangeability ratings before suggesting alternatives.*
CEE: conjugated equine estrogens; HRT: hormone replacement therapy.
Source: References 4, 13-15.

https://www.uspharmacist.com/article/hormone-replacement-therapy-for-menopausal-symptoms

Table 3

Key HRT Counseling Points

Treatment	Counseling Points	Side Effects
All estrogen-containing products	Be aware of signs of PE, DVT, stroke, and MI Report vaginal bleeding Smoking abstinence is important	Common: headache/migraine, nausea and vomiting, stomach cramps, breast pain and tenderness, mood disturbance Severe: CVA, DVT, breast, endometrial, or ovarian cancer, retinal vascular disorder
Conjugated estrogen	Take at the same time every day	
Micronized 17β estradiol Transdermal 17β estradiol IM estrogen	May cause chloasma or melasma, so sunscreen use is important	Common: edema, hirsutism, bloating, withdrawal bleeding
Conjugated estrogen with bazedoxifene	May cause fetal harm Not recommended if breastfeeding Tablet must be swallowed whole	Common: diarrhea, indigestion, dizziness, pain in throat
Depot progestin	Reduces BMD and causes irreversible bone loss Should not be used for >2 y Report any unexplained partial or complete loss of vision	Common: injection-site reaction, weight change, abdominal pain, cholestatic jaundice, dizziness, headache, nervousness, amenorrhea, reduced libido, fatigue Severe: decreased BMD, bone fracture
Combination estrogen-progestin	Application-site reactions Do not place transdermal products on the breast or waistline, rotate application site, and allow ≥1 wk between applications to a particular site Do not expose patches to the sun for prolonged periods of time	Common: application-site reaction, depression, vaginal bleeding, upper respiratory infection Severe: MI, disorders of gallbladder

BMD: bone mineral density; CVA: cerebrovascular accident; DVT: deep venous thrombosis; HRT: hormone replacement therapy; MI: myocardial infarction; PE: pulmonary embolism. Source: Reference 15.

https://www.uspharmacist.com/article/hormone-replacement-therapy-for-menopausal-symptoms

Clinical Trial > Nutr Cancer. 2004;50(2):161-7. doi: 10.1207/s15327914nc5002_5.

Pilot study: effect of 3,3'-diindolylmethane supplements on urinary hormone metabolites in postmenopausal women with a history of early-stage breast cancer

Kathie M Dalessandri [1], Gary L Firestone, Mark D Fitch, H Leon Bradlow, Leonard F Bjeldanes

https://pubmed.ncbi.nlm.nih.gov/15623462/

Review > Nutr Rev. 2016 Jul;74(7):432-43. doi: 10.1093/nutrit/nuw010. Epub 2016 May 31.

Chemopreventive properties of 3,3'-diindolylmethane in breast cancer: evidence from experimental and human studies

Cynthia A Thomson [1], Emily Ho [2], Meghan B Strom [2]

chemoprevention. This review focuses on 3,3'-diindolylmethane (DIM), the major bioactive indole in crucifers. Research of the cancer-preventive activity of DIM has yielded basic mechanistic, animal, and human trial data. Further, this body of evidence is largely supported by observational studies. Bioactive DIM has demonstrated chemopreventive activity in all stages of breast cancer carcinogenesis. This review describes current evidence related to the metabolism and mechanisms

Targeted Support Structures:

Phase 1:

Targeted Support Structures:

Phase 2:

Targeted Support Structures:

Phase 2:

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