BREAST HEALTH AND HORMONES: GOING BEYOND CANCER PREVENTION

Lauren Young, ND

OBJECTIVES

The importance of breast wellness, not just breast cancer treatment

Role of hormones and their metabolites with breast health

How to modify your hormones and improve breast health

WHY TALK BREAST HEALTH?

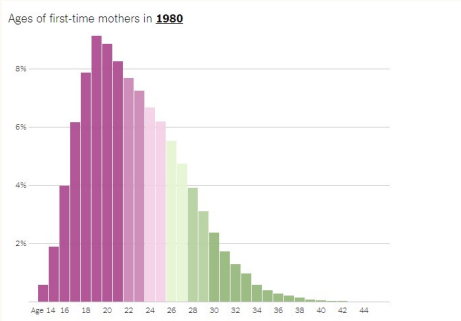
- 1 in 8 women in the US will develop breast cancer
- Increasing 0.5% a year
- 3.8 million women in the US are breast cancer survivors

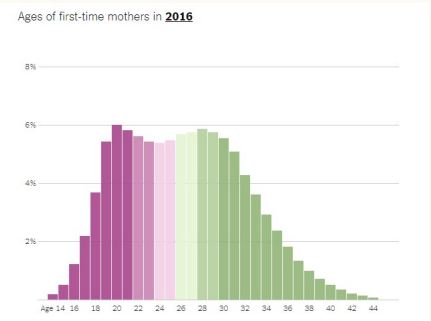
- Deaths from Breast Cancer have declined since 1989- over decline of 43%

"Breast Cancer Statistics: How Common Is Breast Cancer?" Breast Cancer Statistics | How Common Is Breast Cancer? | American Cancer Society, www.cancer.org/cancer/types/breast-cancer/about/how-common-is-breast-cancer.html. Accessed 2 Aug. 2023.

INCREASE RISKS TO BREAST TISSUE

- Delay in motherhood
- Less women becoming mothers
- Increased exposure to Xenobiotics
- HRT use
- Obesity
- Alcohol





PREVENTION: SCREENING TOOLS

- Mammogram
- Thermogram
- Ultrasound
- MRI
- Self Exams
- FNA

MINDFUL OF TRANSGENDER PATIENTS RISK

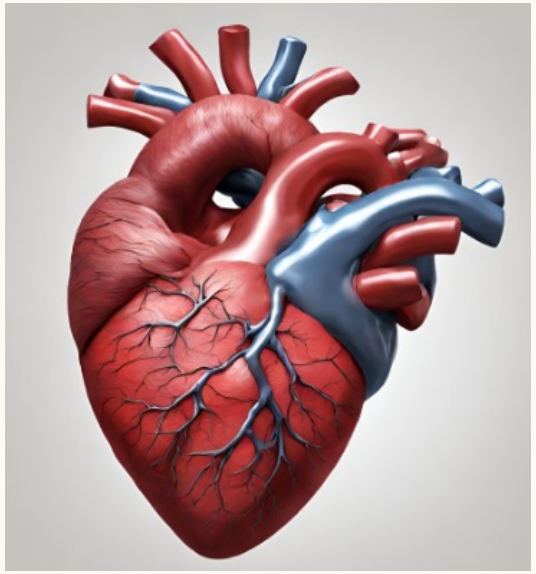
Gender affirming care may alter the risk for breast cancer in patients

- Transmasculine patient- decreased risk with hormone therapy
- Transfeminine patient- increased risk with hormone therapy

ACR breast cancer screening recommendations for transfeminine (male-to-female) people		
Age, use of gender-affirming hormone treatment and breast cancer risk	Mammography	Breast MRI or breast ultrasound
Ages 40 and older, with past or current hormone use for 5 years or more **and** at average risk of breast cancer	May be appropriate	Not recommended
Any age, with no hormone use or less than 5 years of hormone use **and** at average risk of breast cancer	Not recommended	Not recommended
Ages 25–30, with past or current hormone use for 5 years or more **and** at higher risk of breast cancer	Usually appropriate	Not recommended
Ages 25–30 with no hormone use or less than 5 years of hormone use **and** at higher risk of breast cancer	May be appropriate	Not recommended

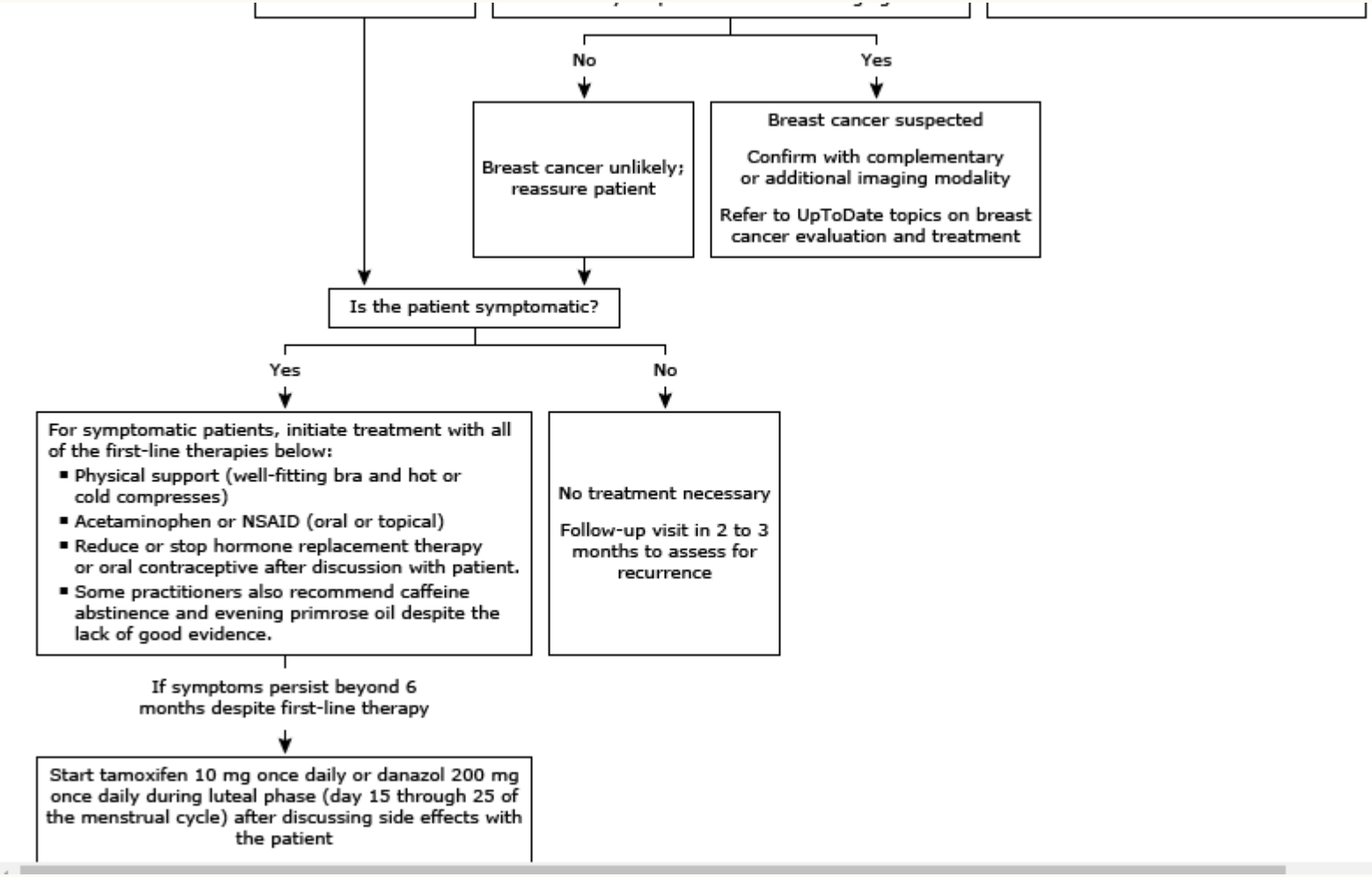
https://www.komen.org/breast-cancer/screening/when-to-screen/transgender-people/

PREVENTION: KEEPING THE TISSUE HEALTHY



LISTENING TO WHAT BREAST TISSUE IS TRYING TO TELL US

CONVENTIONAL TREATMENT OPTIONS FROM UPTODATE



BENIGN BREAST CONDITIONS

There is varied literature, ranging from 30 to 60% of all women. It is most common in women between the ages of 30 to 50 years

Up to 50% risk of developing breast cancer with certain conditions.

Risk Factors:

- obesity
- hormone replacement increases the risk of benign breast diseases.
- a family history of breast cancer has been associated with an increased risk of benign breast diseases, predominantly at premenopausal ages.

NONPROLIFERATIVE

- not associated with an increase risk of breast cancer

- breast cysts
- Galactoceles
- Papillary apocrine changes
- Epithelial related calcifications
- mild hyperplasia

PROLIFERATIVE WITHOUT ATYPIA

1.5 to 2 times that of the general population risk of develeoping breast cancer

- usual ductal hyperplasia
- intraductal papillomas
- sclerosing adenosis
- radial scars
- adenomas
- fibroadenomas
- pseudoangiomatous stromal hyperplasia

ATYPIA HYPERPLASIA

High risk for developing breast cancer

- atypical ductal hyperplasia (ADH)
- atypical lobular hyperplasia (ALH)
- lobular carcinoma in situ (LCIS).

Flat epithelial atypia (FEA) is also an atypical proliferation but does not appear to convey an elevation in cancer risk.

The NEW ENGLAND JOURNAL of MEDICINE

BREAST TISSUE RESPONSES TO HORMONES

ORIGINAL ARTICLE

Benign Breast Disease and the Risk of Breast Cancer

Lynn C. Hartmann, M.D., Thomas A. Sellers, Ph.D., Marlene H. Frost, Ph.D., Wilma L. Lingle, Ph.D., Amy C. Degnim, M.D., Karthik Ghosh, M.D., Robert A. Vierkant, M.A.S., Shaun D. Maloney, B.A., V. Shane Pankratz, Ph.D., David W. Hillman, M.S., Vera J. Suman, Ph.D., Jo Johnson, R.N., et al.

Published in final edited form as:

PMID: 18725513

Cancer Epidemiol Biomarkers Prev. 2008 Sep; 17(9): 2337–2343.

Published online 2008 Aug 25. doi: 10.1158/1055-9965.EPI-08-0380

Estrogen plus Progestin and Risk of Benign Proliferative Breast Disease

Thomas E Rohan,[1] Abdissa Negassa,[1] Rowan T Chlebowski,[2] Norman L. Lasser,[3] Anne McTiernan,[4] Robert S. Schenken,[5] Mindy Ginsberg,[1] Sylvia Wassertheil-Smoller,[1] and David L. Page[6,*]

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Abstract

Go to: ▸

Women with benign proliferative breast disease are at increased risk of subsequent

INCREASED HORMONES; INCREASED DENSITY

"Women with dense tissue in at least 75% of the breast have been shown to have a 4-to 6-fold increase in the risk of subsequent breast cancer (compared to the risk for those with low density)"

A relatively high mammographic density has also been associated with a nine-fold increase in risk of atypical hyperplasia and a twelve-fold increase in risk of hyperplasia without atypia

PROTECTING BREASTS MEANS PAYING ATTENTION TO THEM

- Cyclical symptoms
- Examine hormones
- Monitoring activity of any benign breast lesions

OPPORTUNITY FOR BALANCE

- Address estrogen balance
- Address estrogen metabolites

MEET THE ESTROGENS

Brought to you by an AI photo generator

- Promote growth
- Body development
- Bone growth/prevent loss

Decrease in Estrogen impacts:

- Cardiovascular system
- Insulin resistance
- Lower neurotransmitters
- Connective and reproductive tissues

ESTRADIOL (E2)

- Primarily synthesized by developing follicle in the ovaries
- Reversibly converted into estrone by enzyme 17b- hydroxysteroid dehydrogenase Type II
- Predominate prior to Menopause
- Considered the strongest Estrogen

ESTRONE (E1)

- Primarily synthesized by androstenedione by aromatase conversion in the ovaries, but also the adrenal gland and adipose tissue
- Predominate after Menopause—When your period says "You're on your own" (Estr-OWN)
- Can convert into Estradiol
- More of an affinity to alpha estrogen receptors
- Considered the "weakest" estrogen

ESTRIOL (E3)

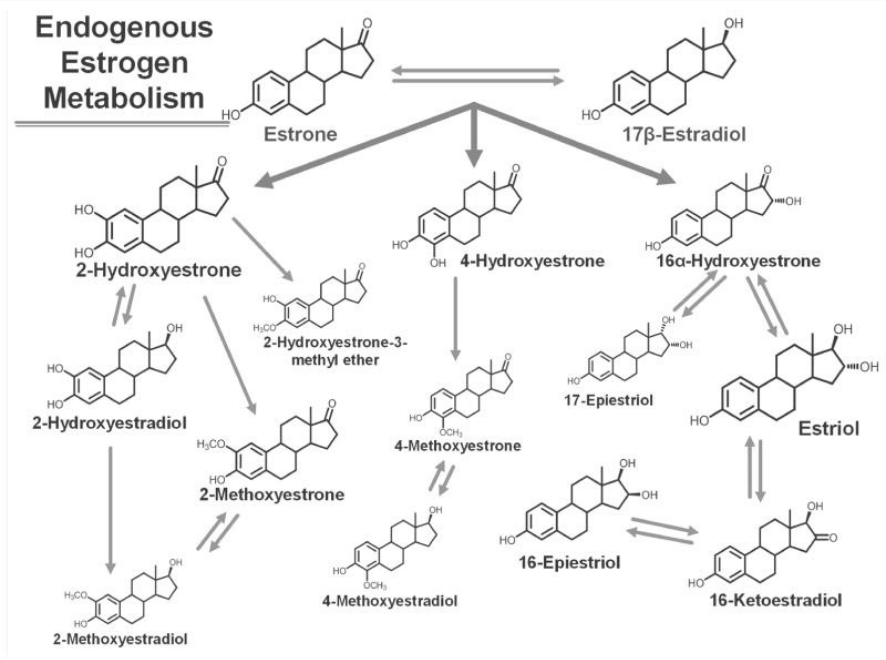
- Synthesized from estrone, which can be converted from the hydroxylation of estradiol or 16-hydroxysterone – often with the placenta
- Elevated during pregnancy
- Considered a weak estrogen
- Utilized in bioidentical hormones
- More of an affinity to beta estrogen receptors

AFFINITY FOR SPECIFIC ESTROGEN RECEPTORS

	Estrogen Receptor-Alpha	Estrogen Receptor-Beta
17- Beta-estradiol	100	100
17- alpha-estradiol	58	11
Estriol	14	21
Estrone	60	37
4-OH-Estradiol	13	7
2-OH-Estrone	2	0.2
Tamoxifen	4	3
Raloxifene	69	16

Boothby, Lisa A., et Al. "Bio identical hormone therapy: a review" in Menopause, 2004, vol 11, No. 3, pp.356-367

A BRIEF HISTORY OF ESTROGEN METABOLITES



URINARY ESTROGEN METABOLITES

1982	1984	1986	1992	1994
16a-OH estrogens are associated with breast cancer and suggested to have an etiological role.	Women with breast or endometrial cancer have increased estrogen 16a hydroxylase activity.	Daily excretion of urinary estrogen metabolites is quantified and total is lowered by dietary fiber.	Evidence that 16a-OH creates genotoxic damage and aberrant proliferation.	Agents that increase 2-OHE1 inhibit carcinogenesis

URINARY ESTROGEN METABOLITES

1995	1995	1996	1997	1999
2:16 ratio is elevated in women and animals with high rates of mammary tumors	Organochlorine pesticides activate CYP enzymes responsible for 16a-OH formation	Daily excretion of urinary estrogen metabolites is quantified and total is lowered by dietary fiber.	Numerous studies showing correlation between favorable outcomes and high 2/16 ratios	Indole-3-Carbinol studied to induce CPY1A1, increase 2-OH and inhibit 4-OH

“WHAT MAN SEES DEPENDS BOTH UPON WHAT HE LOOKS AT AND ALSO UPON WHAT HIS PREVIOUS VISUAL-CONCEPTION EXPERIENCE HAS TAUGHT HIM TO SEE.”

— THOMAS S. KUHN

STUDIES CONTRADICTING THE 2:16 RATIO

2000	2003	2005	2006	2007
"Hormones and Diet in Etiology of Breast Cancer" 2/16 ratio was not associated with reduction of risk. Suggestive of pre- vs post- menopause.	272 women with breast cancer compared to controls, no significant associations with urinary metabolites. Nonsignificant trends were opposite of other studies.	24,697 Danish women – 426 with breast cancer. Found increased cancer risk with 2-OH and lower risk with 16a-OH.	200 women with breast cancer and 200 controls found 2-OHE1 and 16OH were higher in HRT users among breast cancer patients.	Lauren graduated from UBCNM with the assumption that this testing was inconclusive

https://www.townsendletter.com/Jan2013/estrogen0113.html

ENZYME IMMUNOASSAYS (EIA) VERSES LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY (LC-MS/MS)

Review > Steroids. 2015 Jul;99(Pt A):67-75. doi: 10.1016/j.steroids.2015.02.015. Epub 2015 Feb 26.

Epidemiologic studies of estrogen metabolism and breast cancer

Regina G Ziegler [1], Barbara J Fuhrman [2], Steven C Moore [2], Charles E Matthews [2]

Affiliations + expand

PMID: 25725255 PMCID: PMC5722219 DOI: 10.1016/j.steroids.2015.02.015

Free PMC article

Abstract

Early epidemiologic studies of estrogen metabolism measured only 2-hydroxyestrone and 16α-hydroxyestrone and relied on direct enzyme immunoassays without purification steps. Eight breast cancer studies have used these assays with prospectively collected blood or urine samples. Results were inconsistent, and generally not statistically significant; but the assays had limited specificity, especially at the low concentrations characteristic of postmenopausal women. To facilitate continued testing in population-based studies of the multiple laboratory-based hypotheses about the roles of estrogen metabolites, a novel liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay was developed to measure concurrently all 15 estrogens and estrogen metabolites in human serum and urine, as unconjugated and total (glucuronidated+sulfated+unconjugated) concentrations. The assay has high sensitivity (lower limit of quantitation ~1-2 pmol/L), reproducibility (coefficients of variation generally ⩽5%), and accuracy. Three prospective studies utilizing this comprehensive assay

"Women with more extensive hydroxylation along the 2-pathway may have a reduced risk of postmenopausal breast cancer. "

Comparative Study > Breast Cancer Res. 2013 Apr 22;15(2):R34. doi: 10.1186/bcr3416.

Relationship of serum estrogens and estrogen metabolites to postmenopausal breast cancer risk: a nested case-control study

Roni T Falk, Louise A Brinton, Joanne F Dorgan, Barbara J Fuhrman, Timothy D Veenstra, Xia Xu, Gretchen L Gierach

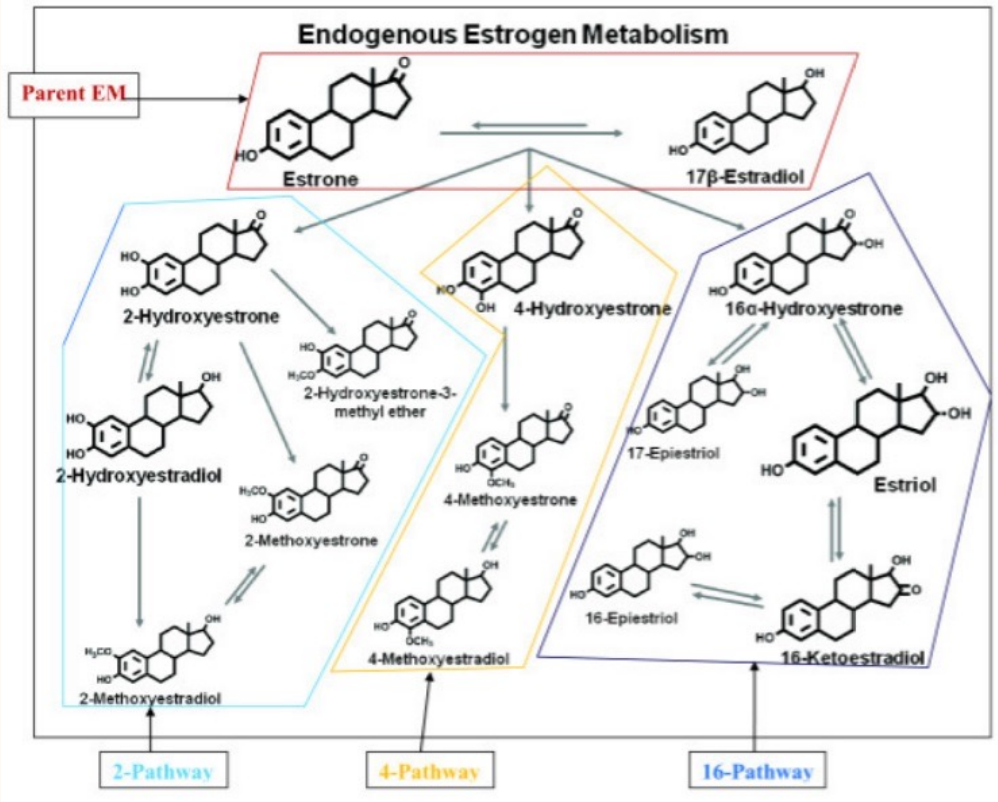
PMID: 23607871 PMCID: PMC4053199 DOI: 10.1186/bcr3416

Free PMC article

Abstract

Introduction: Elevated levels of circulating estrogens are linked to breast cancer risk among postmenopausal women but little is known about the importance of estrogen metabolism. A recently developed liquid chromatography tandem mass spectrometry-based method (LC-MS/MS) measuring a panel of 15 estrogen metabolites (EM) has been evaluated in one study, linking high levels of 2-pathway metabolites relative to the parent estrogens to reduced breast cancer risk. We analyzed this panel of EM in a nested case-control study of postmenopausal breast cancer.

CONCLUSION: METABOLITES ARE IMPORTANT!



THE GOOD, THE BAD AND THE UGLY

2-HYDROXYESTRONE (2-OHE1)

4-HYDROXYESTRONE (4-OHE1)

16A-HYDROXYESTRONE (16A-OHE1)

2-HYDROXYESTRONE (2-OHE1)

"2-OHE1metabolite has very little estrogen receptor binding affinity, and has been shown to decrease cell proliferation by 20 to 30% in cultured breast cancer cell lines."

Comparative Study > Reprod Biol Endocrinol. 2010 Aug 2;8:93. doi: 10.1186/1477-7827-8-93.

Comparison of estrogens and estrogen metabolites in human breast tissue and urine

Emanuela Taioli [1], Annie Im, Xia Xu, Timothy D Veenstra, Gretchen Ahrendt, Seymour Garte

Affiliations + expand

PMID: 20678202 PMCID: PMC2922211 DOI: 10.1186/1477-7827-8-93

Free PMC article

Abstract

Background: An important aspect of the link between estrogen and breast cancer is whether urinary estrogen levels are representative of the intra-tissue levels of bioavailable estrogens.

Methods: This study compares 15 estrogen and estrogen metabolite levels in breast tissue and urine of 9 women with primary breast cancer using a quantitative liquid chromatography-mass spectrometry method.

Results: The average levels of estrogens (estrone, 17 beta-estradiol) were significantly higher in breast tissue than in urine. Both the 2 and the 16-hydroxylation pathways were less represented in breast tissue than urine; no components of the 4-hydroxypathway were detected in breast tissue, while 4-hydroxyestrone was measured in urine. However, the 2/16 ratio was similar in urine and breast tissue. Women carrying the variant CYP1B1 genotype (Leu/Val and Val/Val) showed significantly lower overall

4-HYDROXYESTRONE (4-OHE1)

- Associated with increased breast cancer risk
- Increased amounts found in preparation of adenocarcinoma cells
- More reactive and considered less safe

Comparative Study > Reprod Biol Endocrinol. 2010 Aug 2;8:93. doi: 10.1186/1477-7827-8-93.

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16A-HYDROXYESTRONE (16A-OHE1)

"16a-OHE1 metabolite is a potent estrogenic molecule that activates the ER and induces proliferation of cultured breast cancer cells by 40%."

Comparative Study > Reprod Biol Endocrinol. 2010 Aug 2;8:93. doi: 10.1186/1477-7827-8-93.

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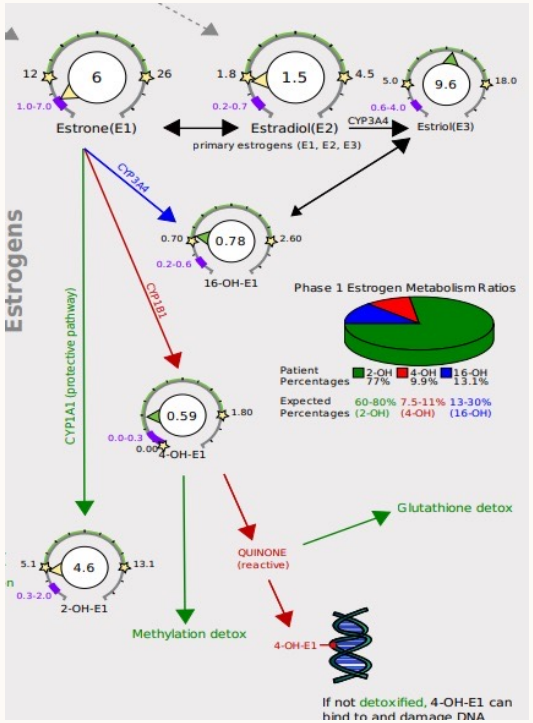
2:16 RATIO

Table 4. Association of Relative Risk Factors for Breast Cancer with 2/16α Ratios

Report	2/16α Ratio	Relative Risk
1 [30]	< 1.80	1.00
	1.80-2.30	0.76
	2.31-2.72	0.60
	2.73-3.29	0.62
	> 3.29	0.55
2 [31]		Odds Ratio
	> 1.91	1.00
	1.38-1.90	1.50
	< 1.38	1.95

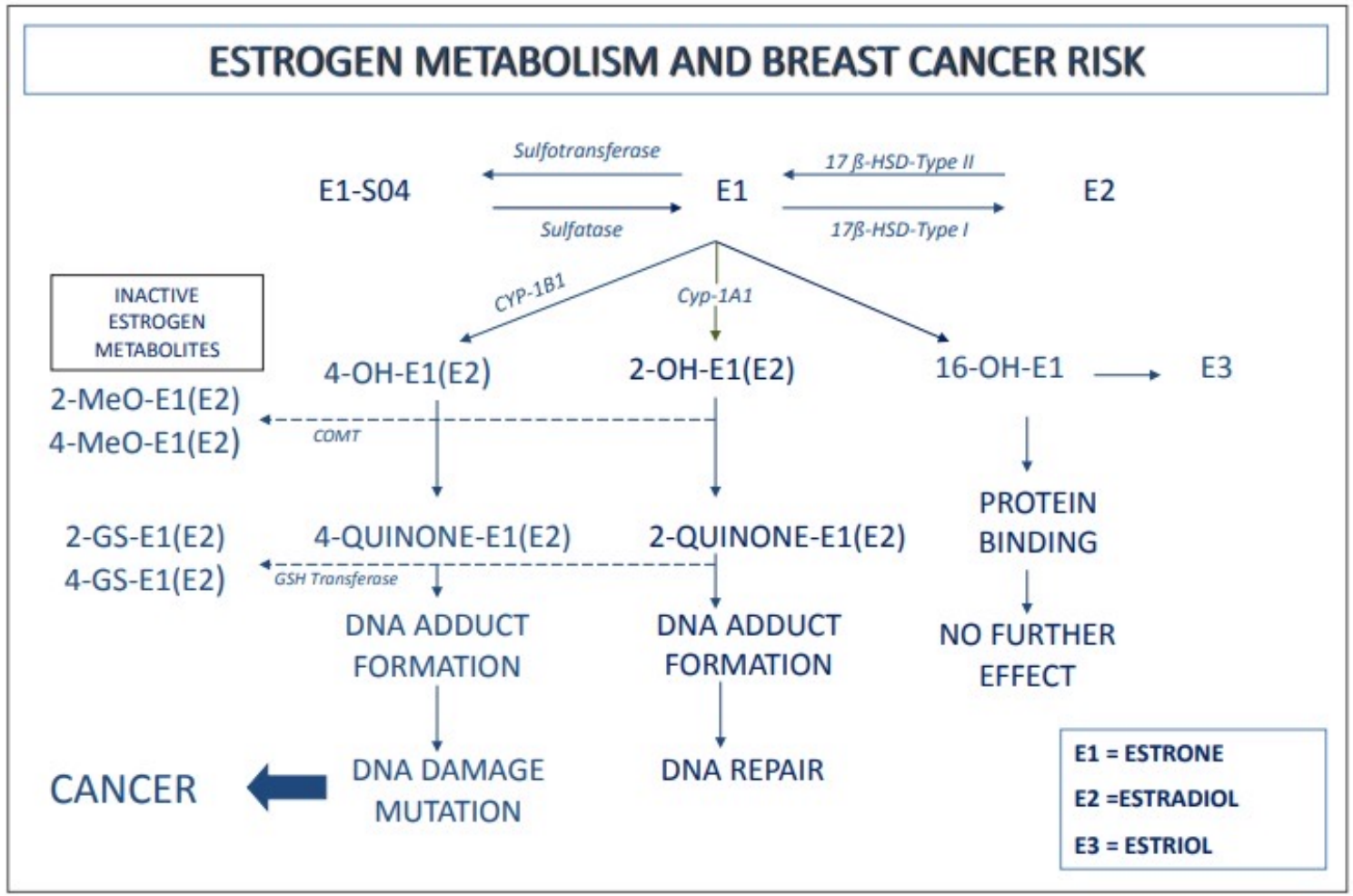
Goals:

- Increasing 2-OHE1
- Lowering 16a-OHE1 and 4-OHE1



SIDE NOTES

- No published literature on urinary estrogen metabolites and risk of breast cancer in women using estrogen replacement therapy
- Pre-menopausal- there isn't a substantial variation in metabolites throughout a woman's cycle. Testing can happen anytime.


ESTROGEN METABOLISM AND BREAST CANCER RISK
Sulfotransferase
17 ß-HSD-Type II
E1-S04
E1
E2
Sulfatase
17ß-HSD-Type I
CYP-1B1
Cyp-1A1
INACTIVE ESTROGEN METABOLITES
4-OH-E1(E2)
2-OH-E1(E2)
16-OH-E1
E3
2-MeO-E1(E2)
4-MeO-E1(E2)
COMT
PROTEIN BINDING
2-GS-E1(E2)
4-GS-E1(E2)
4-QUINONE-E1(E2)
2-QUINONE-E1(E2)
GSH Transferase
DNA ADDUCT FORMATION
DNA ADDUCT FORMATION
NO FURTHER EFFECT
CANCER
DNA DAMAGE MUTATION
DNA REPAIR
E1 = ESTRONE
E2 =ESTRADIOL
E3 = ESTRIOL

MODIFYING OUR RISK

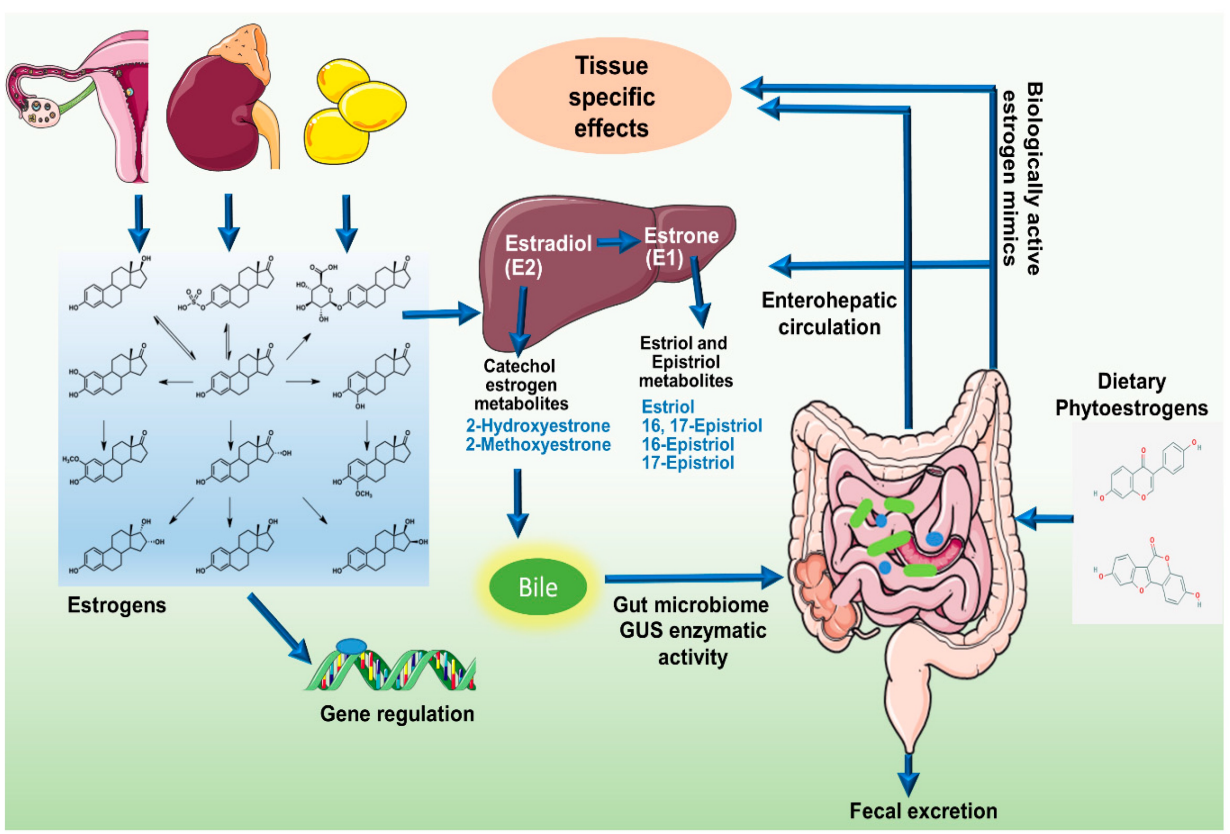
- Reduce exposure to Xenoestrogens
- Support Estrogen Detox
- Ensure Adequate Progesterone
    - Increases conversion of E2 to E1 (17b-hydroxysteroid dehydrogenase)
    - E1 to E1-SO4 (an inert form of estrogen)

ESTROGEN DETOX GOALS

Goals for Prevention:

1. Promote 2- (or even 4-) catechol estrogen pathways
2. Decrease 16-OHE pathway
3. Adequate methylation to avoid conversion to reactive estrogen quinones
4. Adequate glutathione to address any reactive estrogen quinones.

BETA- GLUCURONIDASE



Bifidobacterium & **Calcium-D-Glucarate** have strong inhibiting qualities with Beta-glucuronidase!

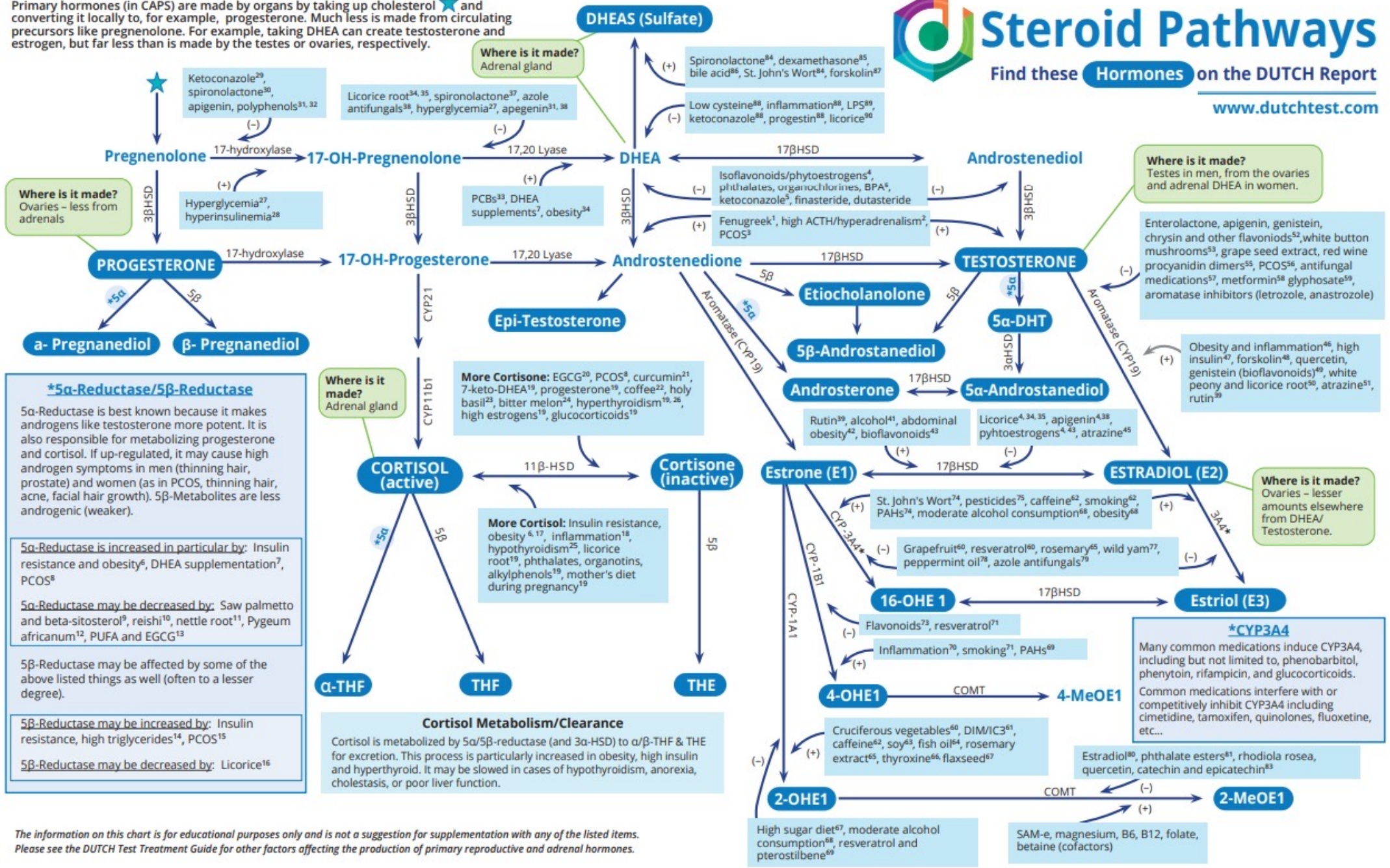
https://doi.org/10.3390/cells8121642
Bouhnik et al., 1996 2. Walaszek et al., 1997

Steroid Pathways

Find these **Hormones** on the DUTCH Report

www.dutchtest.com

Primary hormones (in CAPS) are made by organs by taking up cholesterol ★ and converting it locally to, for example, progesterone. Much less is made from circulating precursors like pregnenolone. For example, taking DHEA can create testosterone and estrogen, but far less than is made by the testes or ovaries, respectively.



*5α-Reductase/5β-Reductase

5α-Reductase is best known because it makes androgens like testosterone more potent. It is also responsible for metabolizing progesterone and cortisol. If up-regulated, it may cause high androgen symptoms in men (thinning hair, prostate) and women (as in PCOS, thinning hair, acne, facial hair growth). 5β-Metabolites are less androgenic (weaker).

5α-Reductase is increased in particular by: Insulin resistance and obesity[6], DHEA supplementation[7], PCOS[8]

5α-Reductase may be decreased by: Saw palmetto and beta-sitosterol[9], reishi[10], nettle root[11], Pygeum africanum[12], PUFA and EGCG[13]

5β-Reductase may be affected by some of the above listed things as well (often to a lesser degree).

5β-Reductase may be increased by: Insulin resistance, high triglycerides[14], PCOS[15]

5β-Reductase may be decreased by: Licorice[16]

Cortisol Metabolism/Clearance

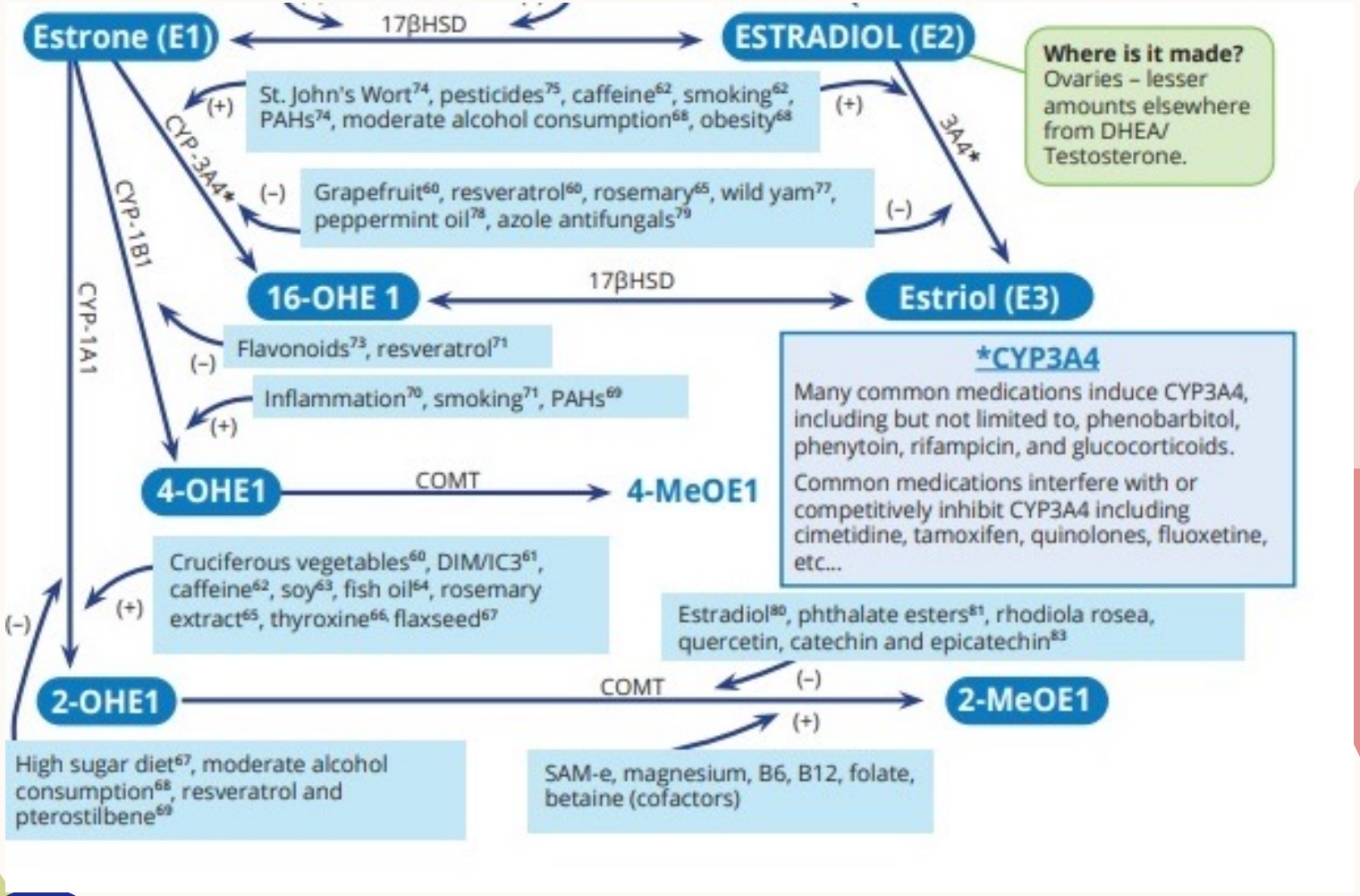
Cortisol is metabolized by 5α/5β-reductase (and 3α-HSD) to α/β-THF & THE for excretion. This process is particularly increased in obesity, high insulin and hyperthyroid. It may be slowed in cases of hypothyroidism, anorexia, cholestasis, or poor liver function.

*CYP3A4

Many common medications induce CYP3A4, including but not limited to, phenobarbitol, phenytoin, rifampicin, and glucocorticoids.

Common medications interfere with or competitively inhibit CYP3A4 including cimetidine, tamoxifen, quinolones, fluoxetine, etc...

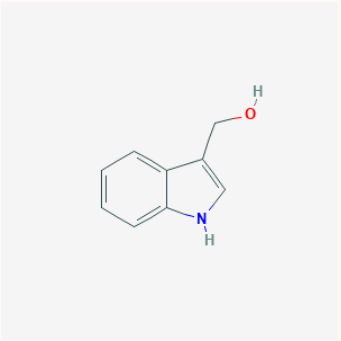
The information on this chart is for educational purposes only and is not a suggestion for supplementation with any of the listed items. Please see the DUTCH Test Treatment Guide for other factors affecting the production of primary reproductive and adrenal hormones.


Estrone (E1)
17βHSD
ESTRADIOL (E2)
Where is it made?
Ovaries – lesser amounts elsewhere from DHEA/ Testosterone.
St. John's Wort[74], pesticides[75], caffeine[62], smoking[62], PAHs[74], moderate alcohol consumption[68], obesity[68]
(+)
(+)
CYP-3A4*
3A4*
(–)
Grapefruit[60], resveratrol[60], rosemary[65], wild yam[77], peppermint oil[78], azole antifungals[79]
(–)
CYP-1B1
CYP-1A1
16-OHE 1
17βHSD
Estriol (E3)
Flavonoids[73], resveratrol[71]
(–)
Inflammation[70], smoking[71], PAHs[69]
(+)
*CYP3A4
Many common medications induce CYP3A4, including but not limited to, phenobarbitol, phenytoin, rifampicin, and glucocorticoids.
Common medications interfere with or competitively inhibit CYP3A4 including cimetidine, tamoxifen, quinolones, fluoxetine, etc...
4-OHE1
COMT
4-MeOE1
Cruciferous vegetables[60], DIM/IC3[61], caffeine[62], soy[63], fish oil[64], rosemary extract[65], thyroxine[66], flaxseed[67]
(+)
(–)
Estradiol[80], phthalate esters[81], rhodiola rosea, quercetin, catechin and epicatechin[83]
2-OHE1
COMT
(–)
(+)
2-MeOE1
High sugar diet[67], moderate alcohol consumption[68], resveratrol and pterostilbene[69]
SAM-e, magnesium, B6, B12, folate, betaine (cofactors)

CRUCIFEROUS VEGETABLES

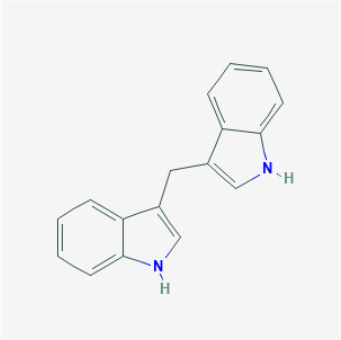
Glucobrassicin + Myrosinase =

INDOLE-3-CARBINOL (I3C)



- Initial substance created with masticating broccoli and other cruciferous vegetables
- Relatively unstable- quickly converts to DIM and other compounds

3,3'-DIINDOLYLMETHANE (DIM)



- Create when I3C encounters acid in our stomachs
- Active component that improves 2:16 ratio

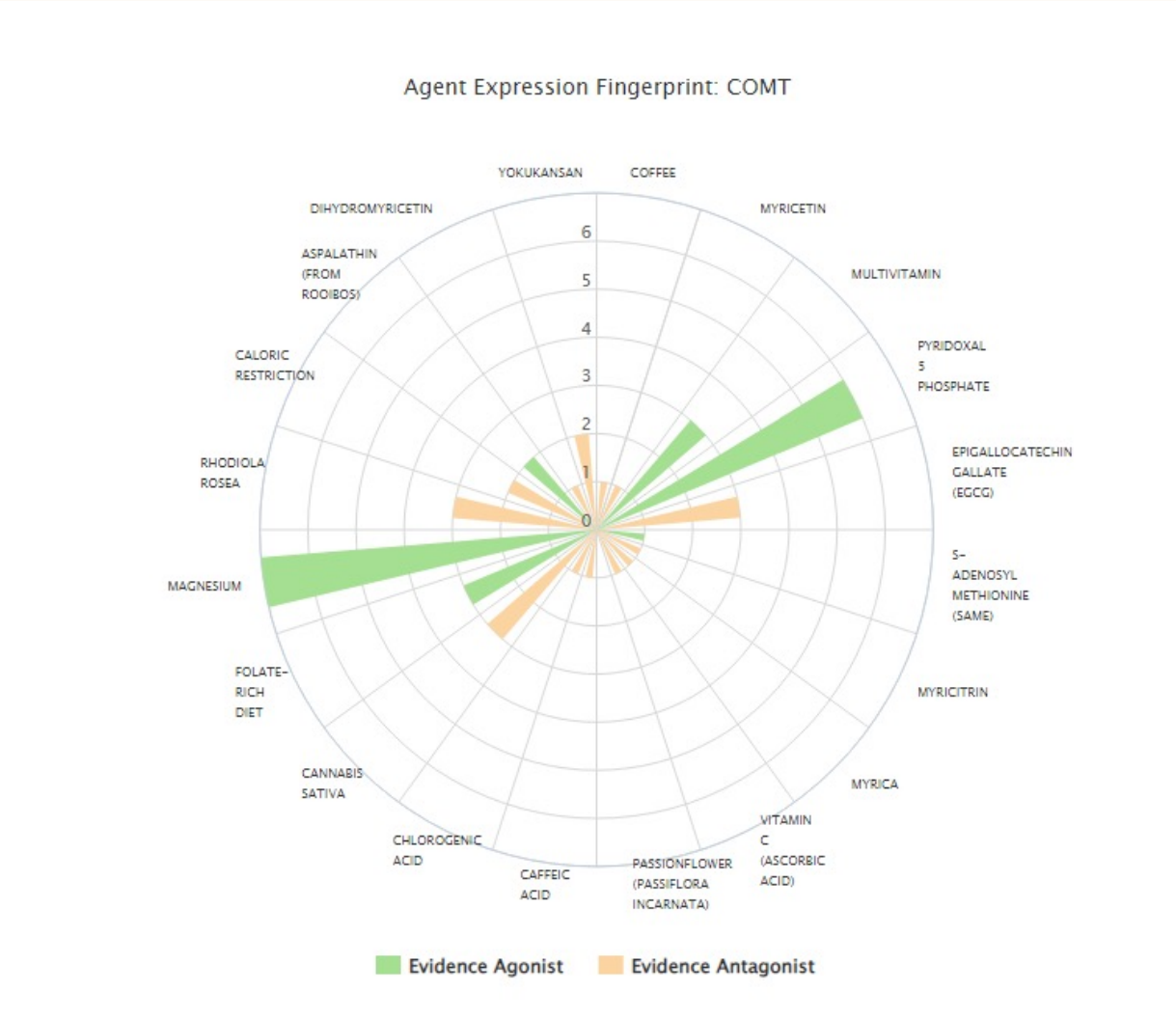
REDUCE EXPOSURE TO ENDOCRINE DISRUPTORS

- Butylated hydroxyanisole, BHA (food preservative)
- Erythrosine (food coloring FD&C Red No. 3)
- Bisphenol A, BPA (polycarbonate plastic denoted as #7, #3 or PC on the recycling symbol)
- Polychlorinated biphenyls, PCBs (electrical oils, lubricants, adhesives, paints)
- Ethinylestradiol (birth control products)
- 4- Methylbenyzlidene camphor, 4-MBC (sunscreen lotions)
- Parabens, commonly known as methylparaben, ethylparaben, propylparaben and butylparaben (cosmetics, lotions and shampoos)

REDUCE EXPOSURE TO ENDOCRINE DISRUPTORS

- Avoid plastics and Styrofoam interacting with foods- IE microwaving or heating
- Use Glass and stainless steel for foods/drinks
- Mindful of ingredients in cleaning supplies, makeup and foods
- Avoid canned foods- follow ewg.org for BPA lined can phase out

SUPPORT COMT



CASE: LAURIE

- 78 yo women with a reoccurrence of ER/PR positive breast cancer a mastectomy 15 years prior
- 2G2P before age 30; no family history of breast cancer
- Retired school teacher. BMI 20
- Diet, sleep and exercise: A+
- Unremarkable medical history

- Previously had done a dried urine test- Poor 2:16 ratio
- Supplements: DIM 1/day, Calcium D-Glucarate 1/day, Magnesium glycinate 1/day, Vitamin D3 +K2 and Fish oil 1 tsp daily
- Doesn't swallow pills! Added these to a green shake daily

LAURIE PART 2

With reoccurrence, wanted to redo testing prior to starting Letrazole.
Looked at Beta-glucuronidase as well as estrogen metabolites.

Persistently low 2/16 ratio.
Beta-glucuronidase was still elevated.

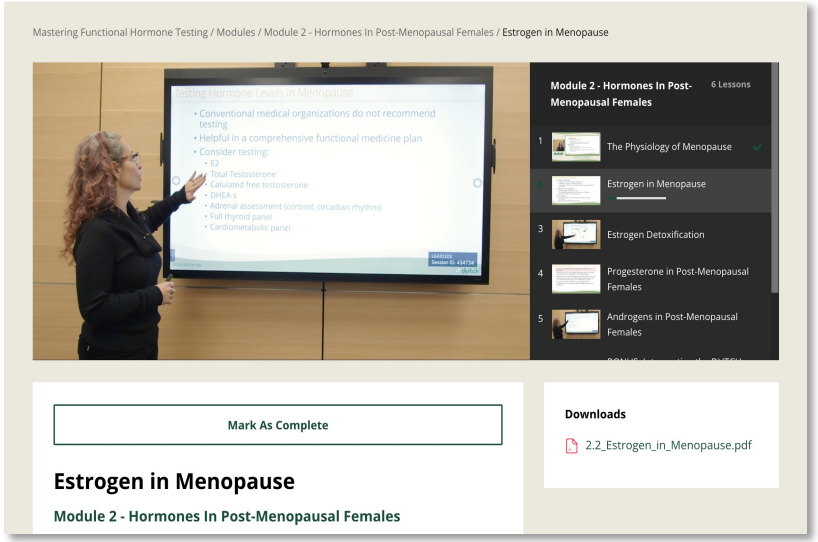
Retesting is important!
She's still doing well and took up boating!

Become a Provider

Exclusive Hormone Education for DUTCH Providers

DUTCH Interpretive Guide

Mastering Functional Hormone Testing Course



Group Mentorship Sessions

Click the Link Below to

Become a DUTCH Provider Today!

RESOURCES

Ziegler RG, Fuhrman BJ, Moore SC, Matthews CE. Epidemiologic studies of estrogen metabolism and breast cancer. Steroids. 2015;9[illegible]-75.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5722219/pdf/nihms677594.pdf

Falk RT, Brinton LA, Dorgan JF, et al. Relationship of serum estrogens and estrogen metabolites to postmenopausal breast cancer risk: a nested case-control study. Breast Cancer

Res. 2013;15(2):R34. Published 2013 Apr 22.

Dallal CM, Tice JA, Buist DS, et al. Estrogen metabolism and breast cancer risk among postmenopausal women: a case-cohort study within B~FIT. Carcinogenesis. 2014;35(2):346- 355.

PubChem. Indole-3-carbinol. https://pubchem.ncbi.nlm.nih.gov/compound/3712 [Accessed October 13, 2020.]

PubChem. 3,3'-Diindolylmethane. https://pubchem.ncbi.nlm.nih.gov/compound/3071 Accessed October 8, 2020.

Reed G, Arneson D, Putnam W, et al. Single-dose and multiple-dose administration of indole-3-carbinol to women: pharmacokinetics based on 3,3'-diindolylmethane. *Cancer Epidemiol Biomarkers Prev* 2006;15(12):2477-2481.

Diindolylmethane (DIM) Information Resource Center - UC Berkeley - Formation. https://www.diindolylmethane-dim.com/formation.htm#.X39kbJpKhPZ [Accessed October 8, 2020]

Lundberg FE, Iliadou AN, Rodriguez-Wallberg K, Gemzell-Danielsson K, Johansson ALV. The risk of breast and gynecological cancer in women with a diagnosis of infertility: a nationwide population-based study. Eur J Epidemiol. 2019 May;34(5):499-507.

McMullen ER, Zoumberos NA, Kleer CG. Metaplastic Breast Carcinoma: Update on Histopathology and Molecular Alterations. Arch Pathol Lab Med. 2019 Dec;143(12):1492-1496.