Uterine Fibroids & DUTCH Testing

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Instagram

drkellyruef

Remember

1. The information in this presentation is provided for informational and educational purposes only and is not medical or treatment advice.

2. Any information and statements regarding dietary or herbal supplements have not been evaluated by the Food and Drug Administration and are not intended to diagnose, treat, cure, or prevent any disease.

3. The use of any information provided in this presentation is solely at your own risk.

Objectives

1. **What** are uterine fibroids?
2. **How** can you utilize information on the DUTCH Test to support clinical outcomes?
3. **Treatment considerations** you can consider as soon as TOMORROW.

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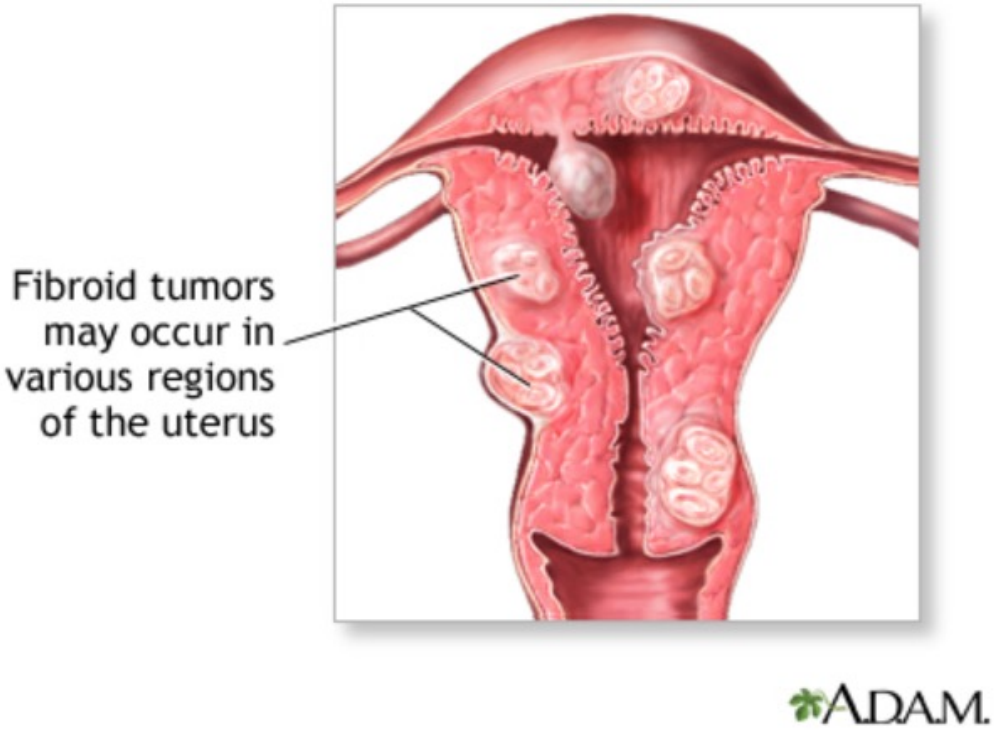
What are uterine fibroids?

Uterine Fibroids (leiomyomas)

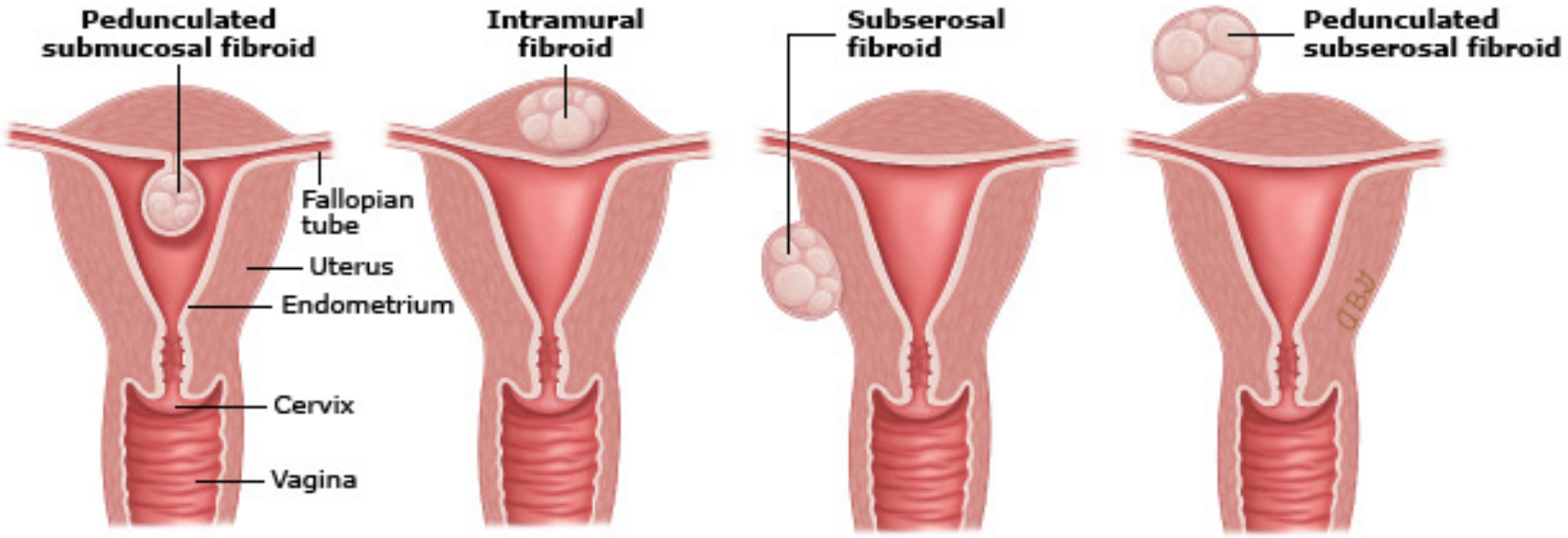
- Solid tumors that grow in the uterus.
- Monoclonal proliferation of a single uterine smooth muscle cell.
- Noncancerous and no increased risk for uterine cancer.



1. Borahay MA, et al. Reprod Sci. 2017 Sep;24(9):1235-1244. PMID: 27872195
2. Jacobson, John D. "Uterine Fibroids." *MedlinePlus*, U.S. National Library of Medicine, 10 Jan. 2022.
3. Szydłowska I, et al. Nutrients. 2022 Feb 9;14(4):734.

Uterine Fibroids (leiomyomas)

They can protrude into the uterine cavity, grow on the outside of the uterus, or grow within the uterine muscle. **Usually there is more than one fibroid at a time**.



Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA. (Accessed on Jan 4th 2023.)

Uterine Fibroid Prevalence

- Affects 1 in 5 women during childbearing years.
- Lifetime prevalence of up to 70%.
- Incidence increases with age until the onset of menopause, then we see a downward trend.
- Significant relationship between the presence of uterine fibroids and coexisting gynecological diseases such as endometrial polyps, endometriosis, and ovarian cysts.

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1. Jacobson, John D. "Uterine Fibroids." *MedlinePlus*, U.S. National Library of Medicine, 10 Jan. 2022.
2. Kınay T, et al. Turk J Obstet Gynecol. 2016 Mar;13(1):31-36.
3. Kwas K, et al. Medicina (Kaunas). 2021 Jul 16;57(7):717.
4. Stewart EA, et al. BJOG. 2017 Sep;124(10):1501-1512.

Signs and Symptoms

Uterine Fibroid Signs & Symptoms

Many women are asymptomatic, but 25-50% of patients may experience one or more of the following:

- Abnormal uterine bleeding (AUB)
  - Heavy menses, clotting, intermenstrual bleeding, menstrual cramping, and anemia.
- Pelvic pain/pressure
- Painful intercourse
- Urinary frequency, difficulty emptying bladder
- Back pain
- Constipation, bloating
- Infertility, adverse pregnancy outcomes

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Heavy menstrual bleeding is now defined as "excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life," instead of the ≥ 80mL blood loss per cycle.

1. Kwas K, et al. Medicina (Kaunas). 2021 Jul 16;57(7):717. PMID: 34356998
2. Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA.
3. Uimari O, et al. Front Reprod Health. 2022 Mar 4;4:818243.

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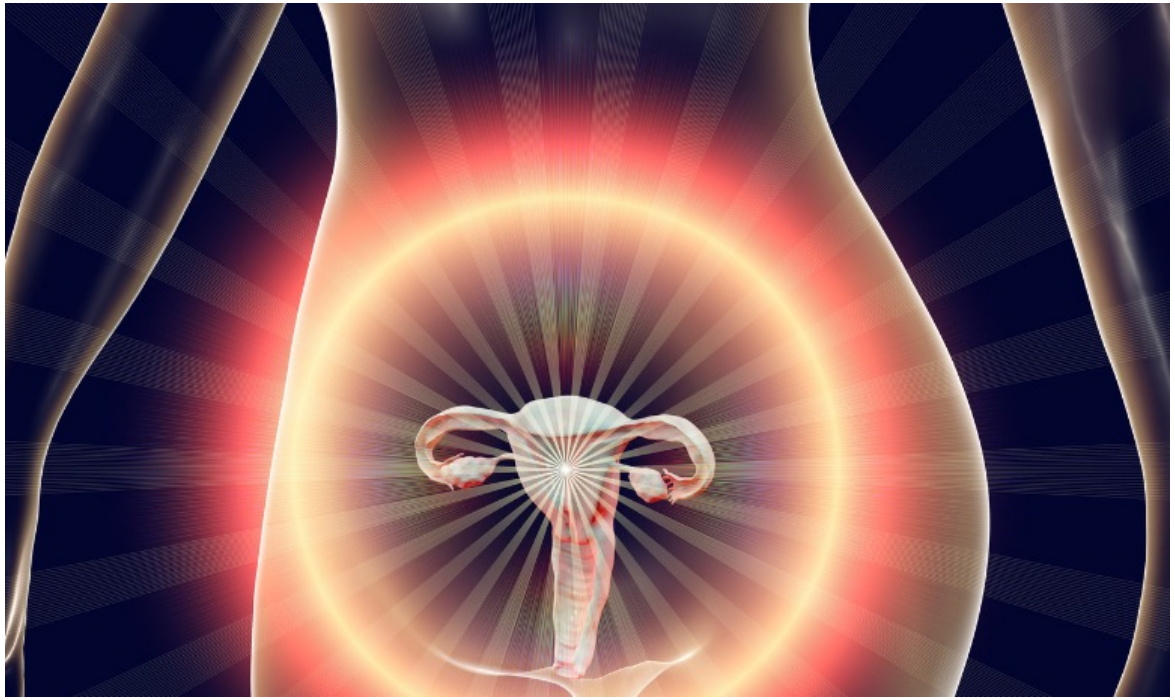
Uterine Fibroid Signs & Symptoms

Symptoms depend on:

1. Number of fibroids
2. Size of fibroid(s)
3. Location of fibroid(s)



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Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA. (Accessed on Jan 4th 2023.)

Uterine Fibroid Size

Some can be very small (rice grain)…

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…others can be very large (melon)

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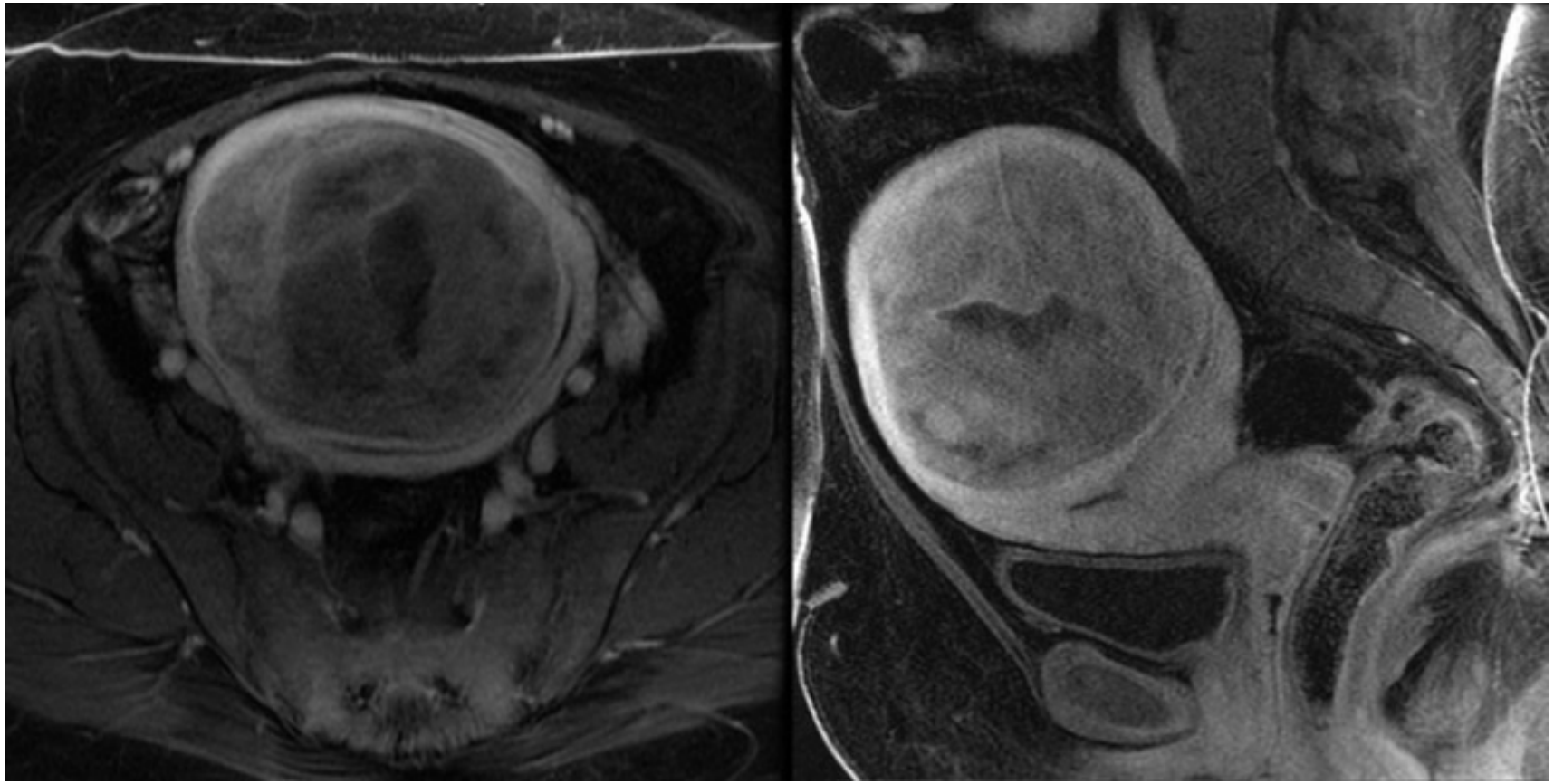
1. Jacobson, John D. “Uterine Fibroids.” *MedlinePlus*, U.S. National Library of Medicine, 10 Jan. 2022.
2. Kınay T, et al. Turk J Obstet Gynecol. 2016 Mar;13(1):31-36.

Uterine Fibroid Size - Example

MRI image of a very large uterine fibroid



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Signs and Symptoms may be due to Coexisting Conditions

"It is important to note that leiomyomas are a common condition, and other coexisting conditions may be the etiology of the presenting symptoms."

-UpToDate

Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA. (Accessed on Jan 4th 2023.)

Pathophysiology

Pathophysiology

- It’s uncertain what causes fibroids.
- Hormones, oxidative stress and genetic factors appear to play a role.
- Various risk factors have been identified.

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Jacobson, John D. “Uterine Fibroids.” *MedlinePlus*, U.S. National Library of Medicine, 10 Jan. 2022.

Estrogen contributes to fibroid growth

Estrogen Receptors and Signaling in Fibroids: Role in Pathobiology and Therapeutic Implications

Abstract

Uterine fibroids are the most common gynecologic tumors with a significant medical and financial burden. Several genetic, hormonal, and biological factors have been shown to contribute to the development and growth of fibroid tumors. Of these factors, estrogen is particularly critical since fibroids are considered estrogen dependent because no prepubertal cases have been described in the literature and tumors tend to regress after menopause. Understanding the role of estrogen in fibroids is not only

Fibroids are estrogen-dependent.

There have been no prepubertal cases.

Fibroids regress after menopause.

Borahay MA, et al. Reprod Sci. 2017 Sep;24(9):1235-1244.

Estrogen contributes to fibroid growth

Impact of Contraception on Uterine Fibroids

symptoms and treatment options are affected by the size, number and location of the fibroids [1]. Fibroids could be single or multiple and may vary in size. **Their growth is estrogen-dependent because they have more estrogen receptors than the surrounding tissue** [2]. It has also been proven that progesterone plays an important role in their pathogenesis, participating in their growth stimulation. It is estimated that uterine fibroids are the most common benign neoplasm occurring

Fibroid tumors have more estrogen receptors than surrounding tissue.

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Kwas K, et al. Medicina (Kaunas). 2021 Jul 16;57(7):717.

Pathophysiology

Estrogen Receptors and Signaling in Fibroids: Role in Pathobiology and Therapeutic Implications

Although plasma estrogen levels are similar in women with and without fibroids, tissue levels are higher in women with fibroids.[47] This correlation illustrates the role of local fibroid aromatase activity in converting androstenedione to estrone, which is then converted to estradiol by 17β-hydroxysteroid dehydrogenase (17β-HSD). Fibroid tissue was found to overexpress both aromatase and 17β-HSD type 1 compared to normal myometrium.[48–50] Therefore, it is not surprising that aromatase inhibitors were shown to inhibit proliferation of leiomyoma cells in experiments and to reduce tumor size in clinical trials.[45,46,51]

Aromatase is overexpressed in fibroid tissue (even more so in black women). This leads to increased aromatization of androgens to estrogen and likely explains why estrogen is higher in fibroid tissue than in serum.

1. Borahay MA, et al. Reprod Sci. 2017 Sep;24(9):1235-1244.
2. Ishikawa H, et al. J Clin Endocrinol Metab. 2009 May;94(5):1752-6.

Progesterone contributes to fibroid growth

Estrogen Receptors and Signaling in Fibroids: Role in Pathobiology and Therapeutic Implications

One of the major roles of estrogen in fibroid development appears to be the induction of progesterone receptor expression through ERα, rendering tumorigenic tissue more responsive to progesterone signals.[52] Using a xenograft fibroid animal model, Ishikawa and colleagues showed that estrogen provides a microenvironment in which progesterone can induce fibroid growth.[53]

Elevated estrogen in fibroid tissue increases progesterone receptor expression, providing "a microenvironment in which progesterone can induce fibroid growth."

Borahay MA, et al. Reprod Sci. 2017 Sep;24(9):1235-1244.

Factors That Increase Risk

Factors That Increase Risk

- Increasing age
- Black race
- Early menarche (<10 years old)
- Oral contraceptives at an early age (13-16 years old)
- Family history of uterine fibroids
- No previous pregnancies/births
- High blood pressure
- Obesity
- Chronic psychological stress

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1. Marshall LM, et al. Fertil Steril. 1998 Sep;70(3):432-9.
2. Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA. (Accessed on Jan 4th 2023.)
3. Kınay T, et al. Turk J Obstet Gynecol. 2016 Mar;13(1):31-36.

Factors That Increase Risk

- Vitamin D deficiency
- Phthalates
- Polychlorinated biphenyls (PCBs)
- Bisphenol A
- Prenatal exposure to diethylstilbestrol (DES)
- Diphenyl Dichloroethene (insecticide)
- Beef and other red meats, ham
- Omega-3s (or environmental pollutants associated with this type of fat)
- Food additive consumption
- Alcohol, especially beer
- High caffeine or coffee intake in women <35 (weak association)

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Plastic water bottles can contain phthalates and BPA.

1. Hunt PA, et al. J Clin Endocrinol Metab. 2016 Apr;101(4):1562-70.
2. Stewart EA, et. al. In: UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA.

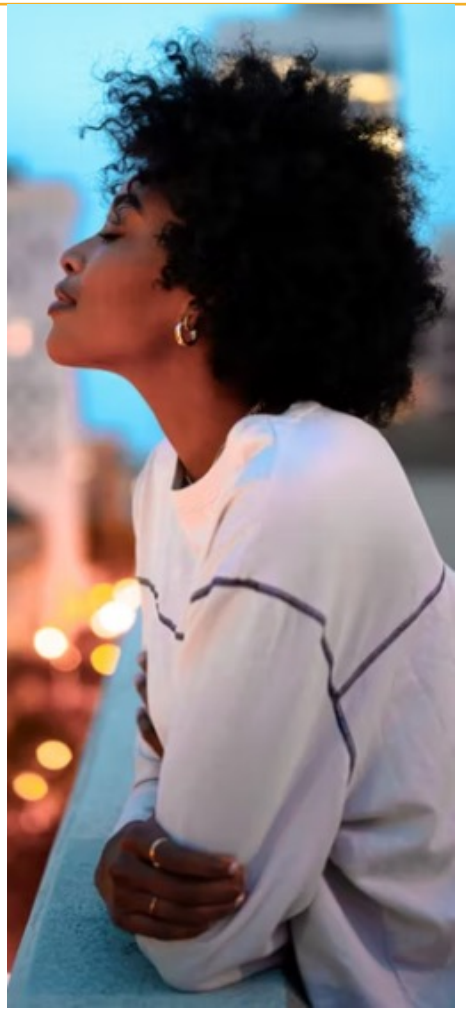
Black Women are Disproportionately Affected

Uterine Fibroids in Black Women

The Health Disparities of Uterine Fibroids for African American Women: A Public Health Issue

Uterine fibroids (leiomyomas) are the most common benign pelvic tumors in women and are the major indication for hysterectomy. **Fibroids are more common and more severe among African American women.** Although this disease disproportionately affects the African American population, we understand little about what causes this disparity. Fibroids should be considered a public health

Also, phthalates tend to be *higher* and vitamin D tends to be *lower* in black women. We will see in upcoming slides that these are risk factors for fibroids!



www.unsplash.com

1. Eltoukhi HM, et al. Am J Obstet Gynecol. 2014 Mar;210(3):194-9.
2. Jacobson, John D. *MedlinePlus*, U.S. National Library of Medicine, 10 Jan. 2022.
3. Raley E, et al. J Allergy Clin Immunol Pract. 2021 Sep;9(9):3290-3292.
4. Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA.

Uterine Fibroids in Black Women

Vitamin D and Risk of Uterine Fibroids

Fibroids are the leading indication for hysterectomy in the United States,[4] and costs exceed six billion dollars annually.[5] There is marked racial/ethnic disparity; blacks have earlier onset,[6] higher incidence,[7] experience more severe symptoms,[8] present with larger tumors,[8] and have a 3-fold higher risk of hysterectomy compared to whites.[9]

Black women tend to be affected by fibroids at a younger age, have larger fibroids, and have a higher risk of hysterectomy than white women.

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Baird DD, et al. Epidemiology. 2013 May;24(3):447-53. PMID: 23493030

Factors That Decrease Risk

Factors that Decrease Risk

- Pregnancy (more pregnancies = decreased risk)
- Long-term use of oral contraceptives (mixed research)
- High physical activity
- Green vegetables
- Fruit (especially citrus fruits)
- Vitamin A from animal sources
- Dairy (2009 large prospective study of black women)

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1. Kwas K, et al. Medicina (Kaunas). 2021 Jul 16;57(7):717.
2. Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA. (Accessed on Jan 4th 2023.)
3. Wise LA, et al. Am J Epidemiol. 2010 Jan 15;171(2):221-32.

Conventional Treatments

Conventional Treatments

- Hysteroscopic resection of submucosal fibroids
- Combined estrogen-progestin contraceptives
- Progestin-releasing IUDs
- Tranexamic acid
- Aromatase inhibitors, SERMs
- GnRH agonists and antagonists
- Uterine artery embolization (UAE)
- Focused ultrasound surgery
- Myomectomy, Hysterectomy

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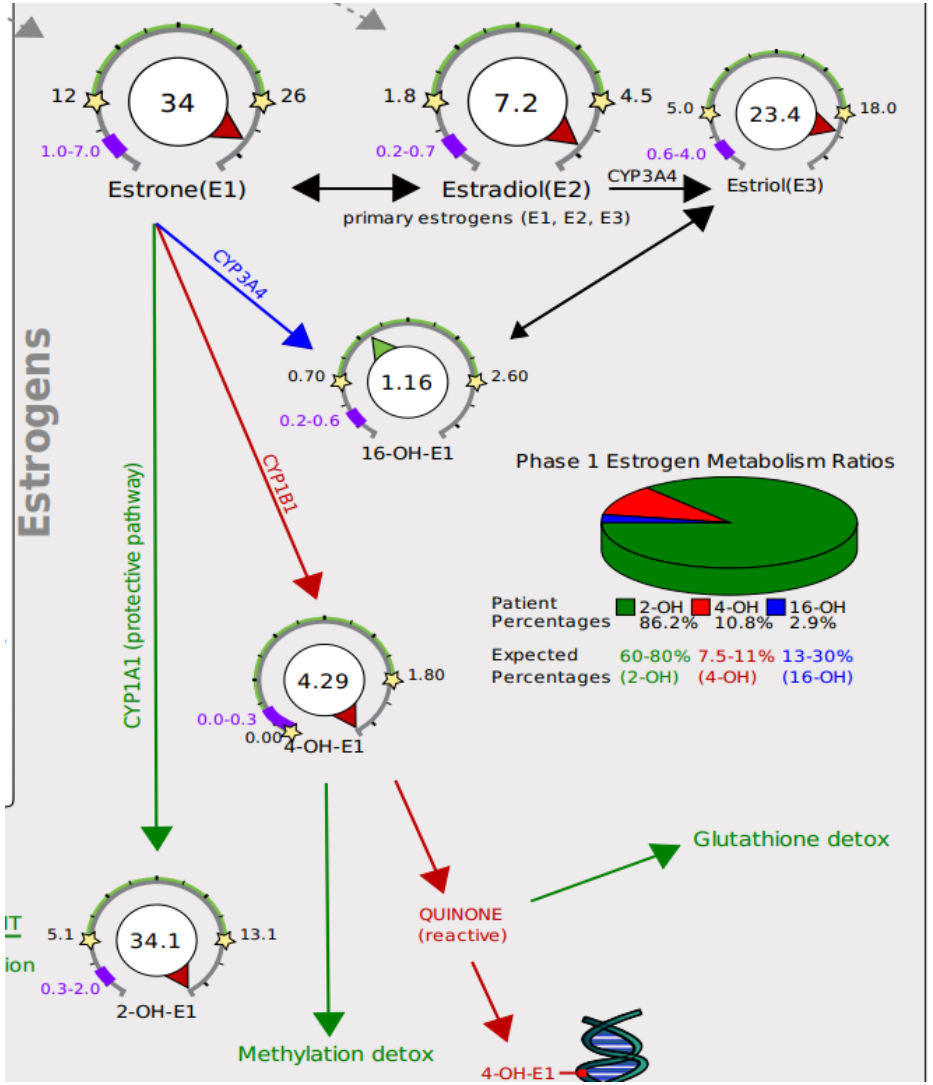
Stewart EA, et. al. UpToDate, Chakrabarti A (Ed), UpToDate, Waltham, MA.

DUTCH Test Patterns Associated With Uterine Fibroids

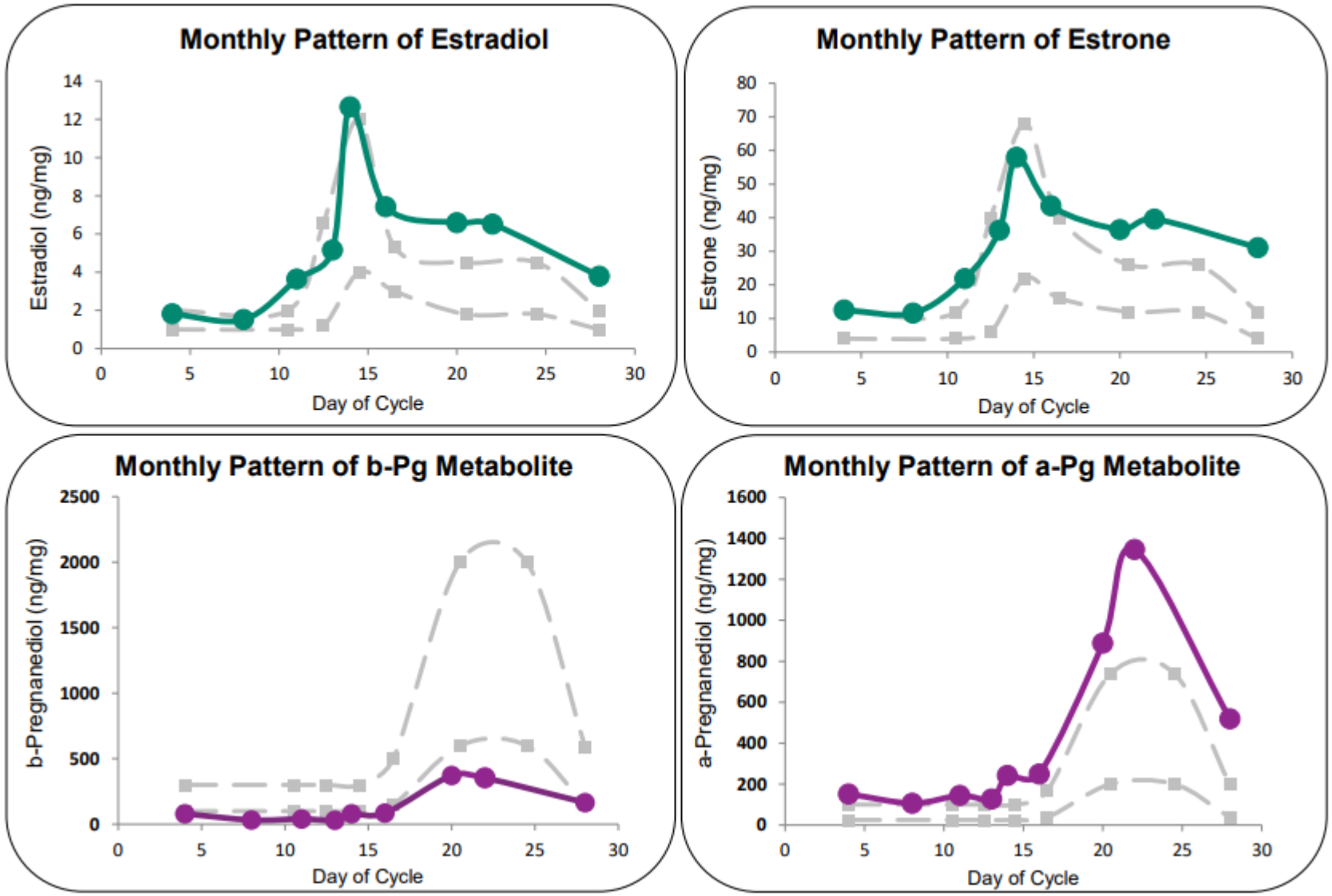
Associated DUTCH Test Patterns: Elevated Estrogen

- As estrogen can fuel the growth of fibroids, it may be helpful to identify elevated estrogen on the DUTCH Test.
- Estradiol (E2) is the most biologically active estrogen in the body, however, estrone (E1) and the phase 1 estrogen metabolites (2-OH, 4-OH, 16-OH) can also bind to estrogen receptors. Thus, it is possible that elevations in any of these markers may contribute to fibroid growth.



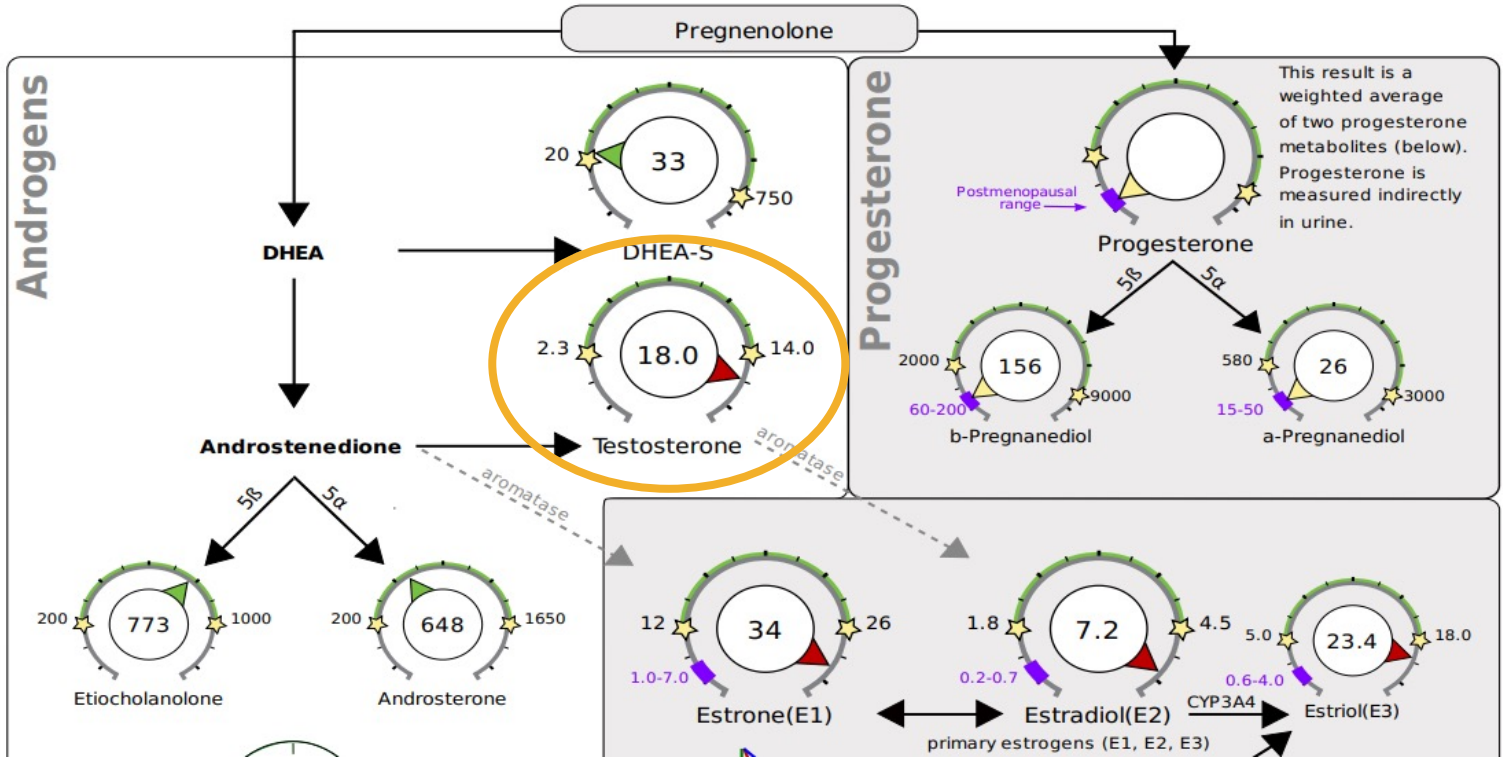
Associated DUTCH Test Patterns: Elevated Estrogen

- Here is an example of estrogen excess on a DUTCH Cycle Mapping report.



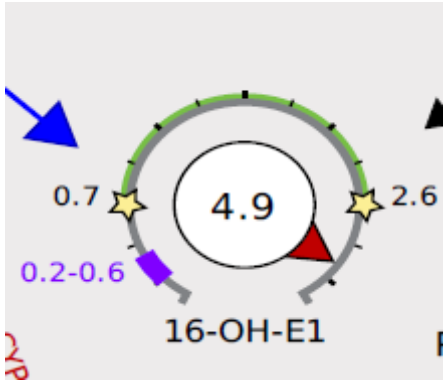
Associated DUTCH Test Patterns: Elevated Androgens

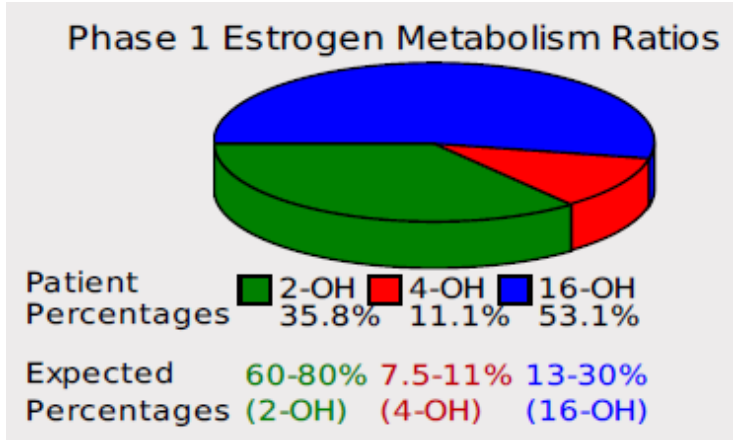
- Because androgens can aromatize to estrogen, elevated androgens may lead to higher estrogen levels.



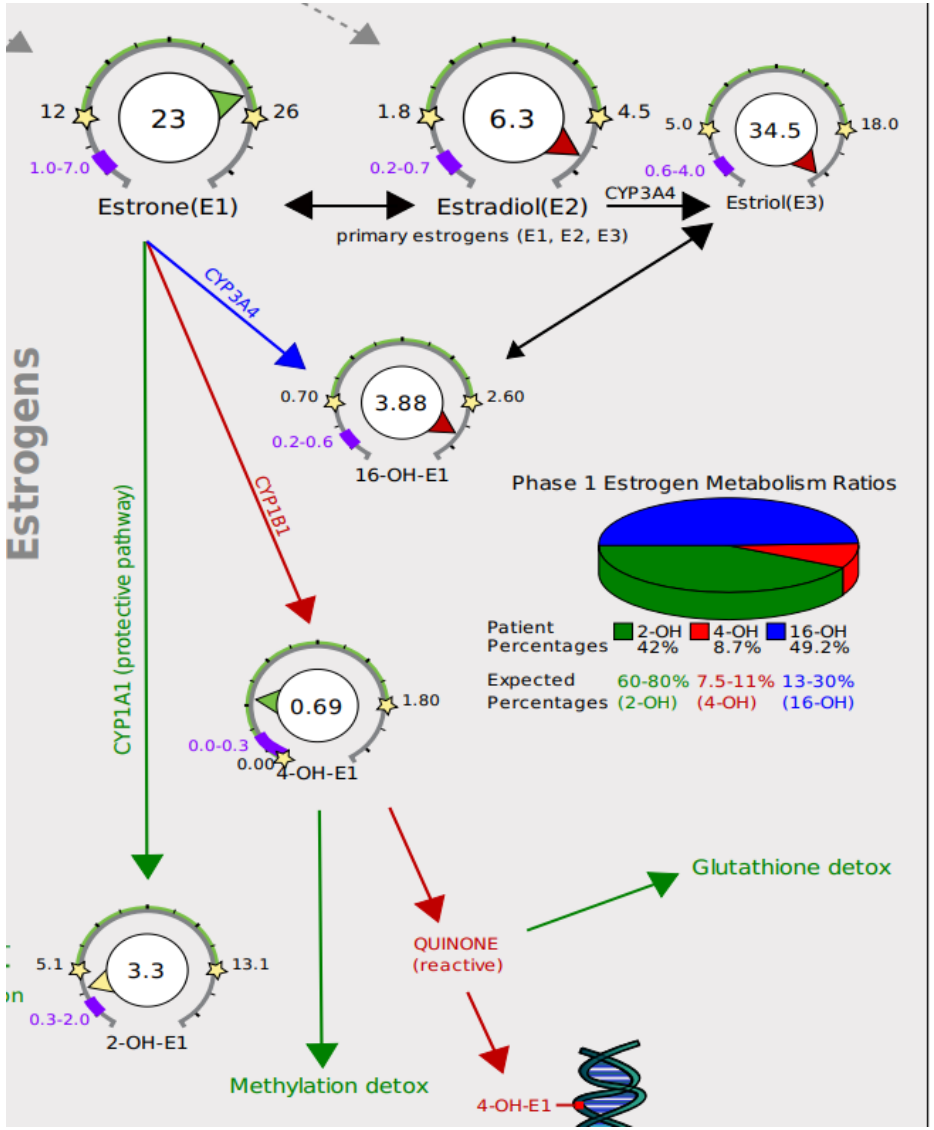
Associated DUTCH Test Patterns: Elevated 16-OH-E1

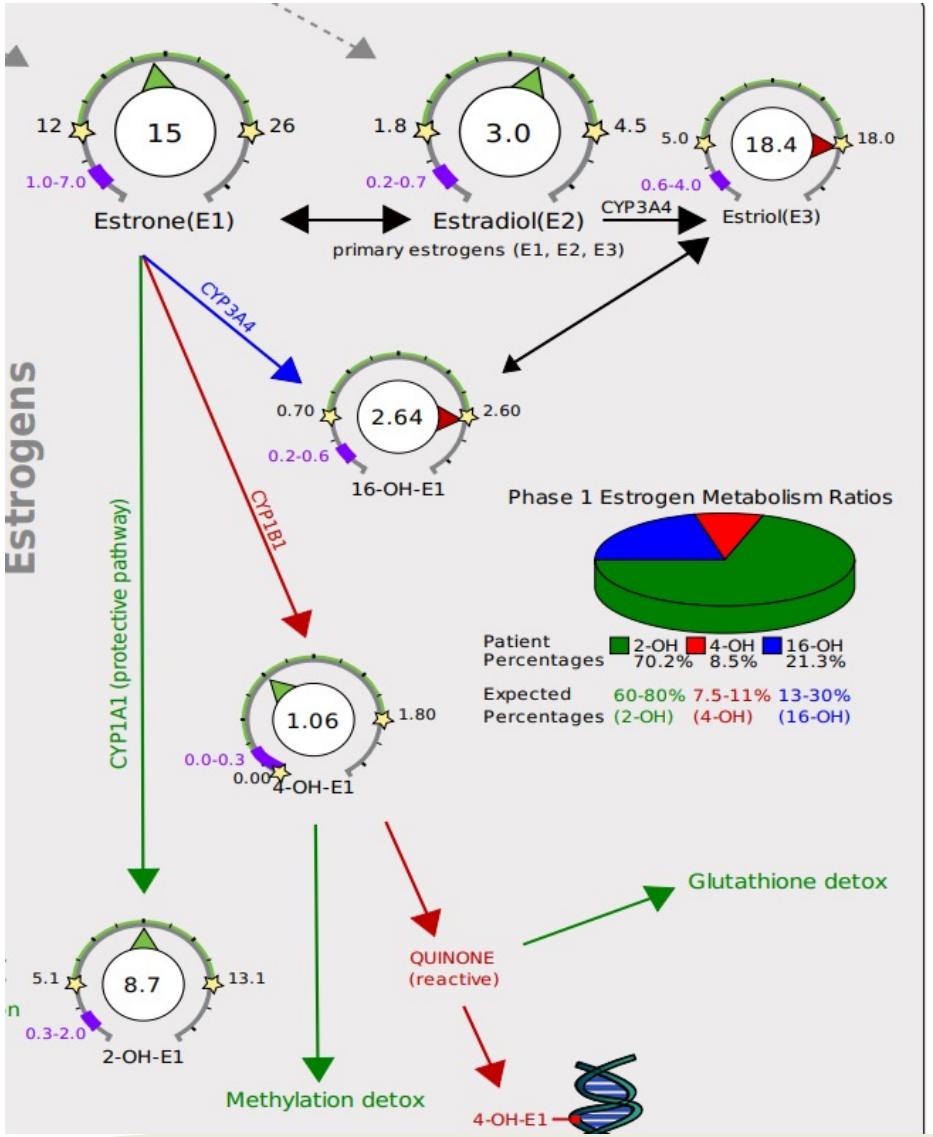
- 16-OH-E1 is a phase 1 estrogen metabolite.
- It is a proliferative estrogen.
- It binds more tightly to estrogen receptors than the 2-OH and 4-OH metabolites.
- If too much estrogen is metabolized into 16-OH-E1, it may contribute to increased fibroid growth, heavy bleeding, breast tenderness, etc.
- CYP3A4 metabolized E1 to 16-OH-E1





Associated DUTCH Test Patterns: Elevated 16-OH-E1





Associated DUTCH Test Patterns: Elevated Quinolinate

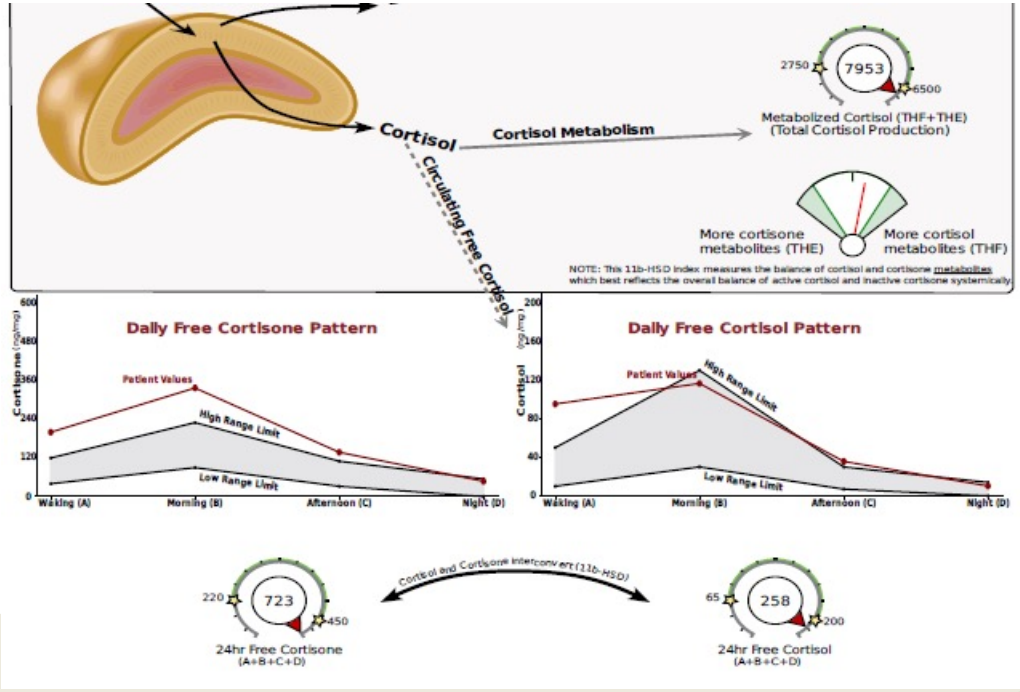
- Urinary phthalate metabolite concentrations have been positively correlated with urinary quinolinate concentration. As phthalate exposure is a risk factor for fibroids, quinolinate may be an important organic acid marker on the DUTCH Test to keep an eye on.

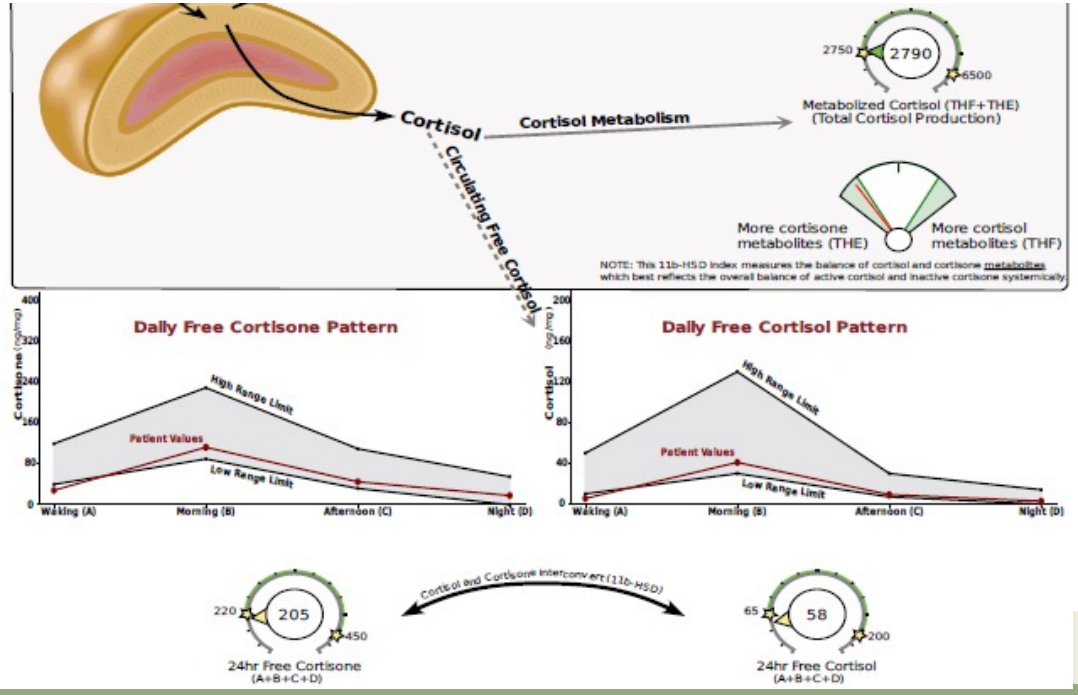
Neuroinflammation Marker - (Urine)				
Quinolinate	Above range	12.5	ug/mg	0 - 9.6

Raley E, et al. J Allergy Clin Immunol Pract. 2021 Sep;9(9):3290-3292.

Associated DUTCH Test Patterns: HPA-axis Dysfunction

- Chronic psychological stress can increase a woman's risk for uterine fibroids, thus it may be helpful when considering treatment and prevention options to assess a woman's HPA-axis health.
- Psychological stress may present as elevated cortisol (more acute) but can also present as low cortisol (more chronic).





Associated DUTCH Test Patterns: Obesity

As obesity is a risk factor for fibroids, it may be helpful to identify if there are any patterns often seen with obesity on the DUTCH Test, such as:

1. Elevated estrogen
2. 5a-reductase upregulated
3. Aromatase upregulated (T and Androstenedione -> E2 and E1, respectively)
4. Estrogen clearance favoring 16-OH-E1
5. Elevated cortisol metabolism
6. Low free cortisol
7. Cortisol metabolism favoring THF when acute and THE when chronic
8. Elevated methylmalonate (deficient B12)
9. Low melatonin

Abstract

The circadian nature of melatonin has a protective effect on the progression of female reproductive cancers, including breast and ovarian cancers. However, the effect of melatonin on the growth of uterine leiomyoma is still unclear. In this study, we found that the growth of uterine leiomyoma ELT3 cells was reduced by treatment with melatonin. Treatment with melatonin increased the distribution of

Lin PH, et al. J Pineal Res. 2020 Jan;68(1):e12620.

Functional Medicine Treatment Considerations

Goals of Functional Medicine Treatment

1. Refer for conventional treatment when appropriate – know that some fibroids cannot be managed with natural medicine alone.
2. Improve symptoms.
3. Stabilize growth (*hope* for regression!) until the woman enters menopause.

Summary of Functional Medicine Treatment Considerations

- Lower estrogen if elevated (by avoiding contributors and improving detox).
- Lower 16-OH-E1 if elevated.
- Lower androgens (T, DHEA, etc.) if elevated.
- Reduce stress and support hypothalamic-pituitary-adrenal (HPA) axis.
- Avoid things that increase risk for fibroid occurrence and growth.
- Encourage things that lower risk for fibroid occurrence and growth.

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Lower Estrogen if Elevated

Contributors to Elevated Estrogen

- Being overweight
- Diabetes / blood sugar dysregulation
- PCOS
- Age (perimenopause)
- Thyroid issues
- Increased aromatase activity
- Endocrine disrupting chemicals (EDCs), Xenoestrogens!
- Alcohol
- Suboptimal liver clearance
- Gut dysbiosis
  - (e.g., elevated b-glucuronidase)
- Estrogen, DHEA and/or testosterone supplementation
- Elevated androgens (T, DHEA, etc.)
- Low SHBG
  - Often seen in obesity, insulin resistance (IR), metabolic disorder, fatty liver, PCOS, sleep apnea, hypothyroidism, Cushing's, etc.
- High inflammation
- High stress
- Ovarian cyst(s)

Considerations for Supporting Estrogen Detoxification

- Diindolylmethane (DIM)
  - Lowers circulating estrogens and tends to improve CYP1A1 (towards 2-OH) metabolism
- Indole-3-carbinol (I3C)
  - Needs stomach acid to convert properly to DIM
- Cruciferous vegetables
- Apiaceae family vegetables
  - Carrots, celery, parsley, coriander, etc.
- Rosemary
- Turmeric/curcumin

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Considerations: Curcumin

Curcumin inhibits human leiomyoma xenograft tumor growth and induces dissolution of the extracellular matrix

Result(s): We found that curcumin was well tolerated as a dietary supplement, free curcumin and its metabolites were detected in the serum, and exposure resulted in approximately 60% less leiomyoma xenograft growth as well as dissolution of the peripheral extracellular matrix architecture of the xenografts. The production of matrix proteins, including collagens, decreased, whereas the number of apoptotic cells in the xenografts increased. Additionally, when xenografts were placed in a uterine intramural location, we found a significantly increased apoptotic response to curcumin in the diet.

Conclusion(s): Mice on a diet supplemented with curcumin could achieve serum concentrations sufficient to regulate human leiomyoma xenograft growth, and curcumin could play both preventive and curative roles in the treatment of uterine leiomyoma as an oral nutritional supplement.

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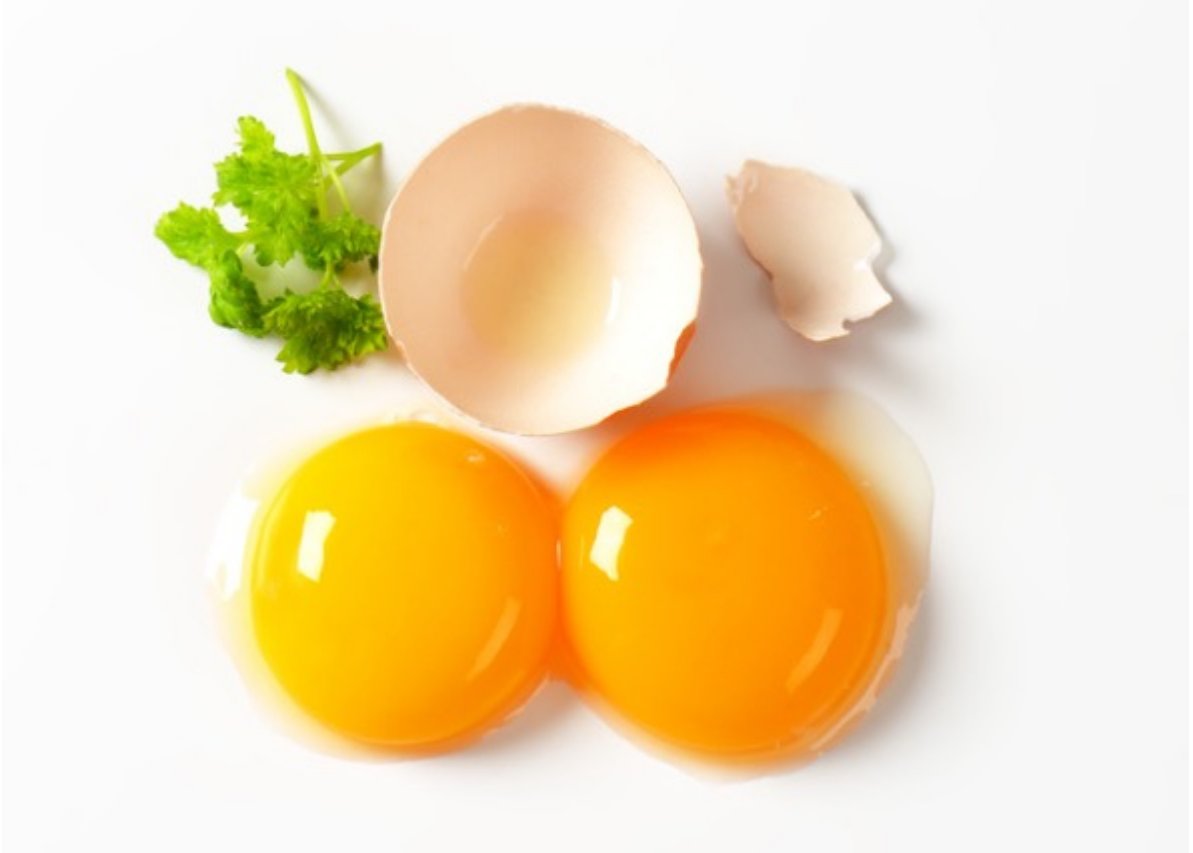
Malik M, et al. F S Sci. 2023 Feb;4(1):74-89.

Considerations for Supporting Estrogen Detoxification

- Sulforaphane/glucoraphanin
  - Highest in broccoli seed sprouts
- Calcium-D-glucurate
  - May improve estrogen and androgen clearance in the stool (phase 3)
- Resveratrol
- Glutathione/N-acetyl-cysteine (NAC)
- Magnesium
- B-vitamins
- Choline/trimethylglycine (TMG)
- SAMe



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Lower 16-OH-E1 if Elevated

Considerations for Lowering 16-OH-E1

- Avoiding things that upregulate CYP3A4:
  - St. John's wort
  - Caffeine and smoking
  - Pesticides
  - Obesity and moderate alcohol consumption
  - Polycyclic aromatic hydrocarbons (PAHs)
  - Medications (phenobarbital, phenytoin, rifampicin, dexamethasone, etc.)

www.unsplash.com

PAHs are produced when gasoline, oil, coal, wood, garbage, or tobacco are burned. PAHs are found in the air, water, and soil and can stick around for months to years.

1. Bradlow HL, et al. Environ Health Perspect. 1995 Oct;103 Suppl 7(Suppl 7):147-50.
2. Luckert C, et al. Toxicol Lett. 2013 Oct 24;222(2):180-8.
3. Mahabir S, et al. Cancer Med. 2017 Oct;6(10):2419-2423.
4. Sowers MR, et al. J Nutr. 2006 Jun;136(6):1588-95.
5. Whitten DL, et al. Br J Clin Pharmacol. 2006 Nov;62(5):512-26.

Reduce PAH Exposure

- Limit inhalation of gasoline fumes.
- Limit inhalation of smoke from wood fires.
- Limit foods that are smoked, grilled, and charred over a fire, and limit fried foods.
- Limit inhalation of fumes from oil heated at high temps.
- Avoid shampoos and cosmetics containing coal tar.
- Avoid mothballs containing naphthalene.
- Consider an indoor air purifier.

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"PAHs concentrations in smoked fish are the product of both sea pollution and the smoking process."

1. Visciano P, et al. J Food Prot. 2006 May;69(5):1134-8.
2. Yao Z, et al. Environ Sci Pollut Res Int. 2015 Oct;22(20):16110-20.

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Considerations for Lowering 16-OH-E1

- CYP3A4 inhibitors:
  - Grapefruit, resveratrol, rosemary, wild yam, peppermint oil, Azole antifungals, thyroid hormone
- Use caution when using CYP3A4 inhibitors, as CYP3A4 plays a major role in the detoxification of many pharmaceutical drugs, toxins, and waste products.

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1. Debersac P, et al. Food Chem Toxicol. 2001 Sep;39(9):907-18.
2. Dresser GK, et al. Clin Pharmacol Ther. 2002 Sep;72(3):247-55.
3. Hodges RE, et al. J Nutr Metab. 2015;2015:760689.
4. Niwa T, et al. Curr Drug Metab. 2014;15(7):651-79.
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6. Wu WH, et al. J Am Coll Nutr. 2005 Aug;24(4):235-43.

Resveratrol may Suppress Fibroid Growth

Natural Antioxidant Resveratrol Suppresses Uterine Fibroid Cell Growth and Extracellular Matrix Formation In Vitro and In Vivo

phase. Our findings indicated the inhibitory effects of RSV on the ELT-3-LUC xenograft model and indicated that RSV reduced ECM-related protein expression in primary human leiomyoma cells, demonstrating its potential as an anti-fibrotic therapy for UF.

Resveratrol may help slow fibroid growth!

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Chen HY, et al. Antioxidants (Basel). 2019 Apr 12;8(4):99.

Resveratrol

- Inhibits CYP3A4 (decreases 16-OH-E1 production).
- Inhibits CYP1B1 (decreases 4-OH production).
- Induces quinone reductase which may help reduce estrogen semi-quinones back into catechol estrogens.
- Induces Nrf2 (regulatory pathway that combats oxidative stress by regulating GST, quinone reductase, glutathione reductase, glutathione peroxidase, and thioredoxin reductase).

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Considerations for Lowering 16-OH-E1

Supporting phase 2 clearance of 16-OH-E1 (Sulfation and Glucuronidation)

- Sulfation support:
  - Lower inflammation and treat hypothyroidism, if present
  - Provide sulfur donors such as methionine, N-acetylcysteine (NAC), methylsulfonylmethane (MSM), taurine, sulforaphane, glutathione and sulfurous foods such as onions, garlic, eggs, brassicas, asparagus, arugula, etc.
  - Consider supplementing with the cofactor molybdenum and/or increasing molybdenum rich foods in the diet such as legumes, whole grains, rice, nuts, bananas, leafy vegetables, dairy products, beef, chicken, eggs, etc.

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Considerations for Lowering 16-OH-E1

Supporting phase 2 clearance of 16-OH-E1 (Sulfation and Glucuronidation)

- Glucuronidation support:
  - Sulforaphane, citrus fruits, quercetin, curcumin, calcium-d-glucurate

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Sulforaphane/Glucoraphanin

- Broccoli sprouts have the highest concentration of sulforaphane.
- Sulforaphane supports the detox of phase 1 estrogens (including 16-OH-E1) via sulfation, glucuronidation, and methylation.
- Sulforaphane activates antioxidant pathways.
- Sulforaphane helps to prevent DNA damage by estrogen semi-quinones.
- Note that sulforaphane degrades in our stomach acid, so glucoraphanin (best coupled with myrosinase to activate it to sulforaphane) may be better to supplement with than sulforaphane itself. OR eat broccoli sprouts!

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Basten GP, et al. Carcinogenesis. 2002 Aug;23(8):1399-404.

Considerations for Lowering 16-OH-E1

- Encourage phase 1 estrogen metabolism down CYP1A1 towards 2-OH estrogen catechols, which are the most stable of the phase 1 metabolites:
  - Cruciferous vegetables
  - Apiaceae family (carrot family) vegetables
  - Rosemary
  - Fish oil
  - Avoiding a high sugar diet
  - Avoiding alcohol
  - Soy
  - Flaxseeds

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Lower Androgens if Elevated

Contributors to Elevated Androgens

- Being overweight / high body fat percentage
- Insulin resistance / blood sugar dysregulation
- PCOS
- Thyroid issues
- Slow aromatase activity
- Endocrine disruptors
- Alcohol
- Nicotine
- Suboptimal liver clearance
- Gut dysbiosis
  - (e.g., elevated b-glucuronidase)
- High inflammation
- High stress
- DHEA and/or testosterone supplementation or transference from a partner, caretaker, etc.
- Low SHBG
  - Often seen in obesity, insulin resistance (IR), metabolic disorder, fatty liver, PCOS, sleep apnea, hypothyroidism, Cushing's, etc.
- Non-classical congenital adrenal hyperplasia (NCAH)
- High adrenal output
- High ovarian output

General Liver Support – Your Liver is Your Friend!

- Plays an important role in ALL phases of hormone detox.
  - Phase 1: participates in oxidizing E1 and E2 into phase 1 estrogen metabolites.
  - Phase 2: participates in methylation, sulfation, glucuronidation, etc. of those reactive phase 1 estrogen metabolites.
  - Phase 3: secretes about one quart of bile daily to help clear out estrogens in the stool.
- Liver support:
  - B vitamins, choline, inositol, NAC, ALA, milk thistle, dandelion root, beets, etc. Limit sugar, caffeine, alcohol, and processed foods (that can interfere with B-vitamin metabolism) as these can all adversely affect the liver.

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Fiber

- High fiber diet may help with constipation and bloating seen with uterine fibroids.
- Fiber is also important for phase 3 elimination of hormones from the body.

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Reduce Stress & Support the HPA-Axis

Reduce Stress & Support the HPA-Axis

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https://dutchtest.com/video/cortisol-and-stress-how-to-recover-and-start-strong-this-year/

Avoid Things That Increase Risk

Avoid/Limit Things That Increase Risk for Uterine Fibroids

1. Limit phthalates, BPA, PCBs, and pesticides
2. Limit alcohol, food additives, and caffeine (weak association)
3. Limit red meat and ham (encourage grass-fed, pasture-raised)
4. Lower blood pressure, if elevated
5. Lose weight, if appropriate
6. Avoid omega-3 products from unreputable companies
7. Ensure optimal vitamin D levels
8. Lower stress

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Phthalate Exposure

- Added to plastics to make them durable, pliable, and soft.
- Shampoos, hair spray, soaps, deodorants, nail polish, lotions, plastic packaging, garden hoses, medical tubing, vinyl flooring, lubricating oils, carpet backings, adhesives, and more!
- Higher in Black and Hispanic women (Raley E, et al.).
- Often found in “fragrance.”

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Bisphenol Exposure

- Found in water bottles, juice bottles, food containers, eyeglass lenses, and the linings of food and soda cans.
- Items labeled “BPA-free” may contain other bisphenols (BPS!)
- Found in receipt paper.

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Callahan, Alice. The New York Times, 17 Apr. 2020, https://www.nytimes.com/article/plastics-to-avoid.html.

Polychlorinated Biphenyl (PCB) Exposure

- Manmade (Mansanto Inc.) chemicals found in the air, soil, and water that were banned in the US in 1977.
- However, leach from landfills and hazardous waste sites into our water.
- Can take decades or longer to break down.
- Higher levels are found in fish, especially catfish, buffalo, and carp.
- Plants don’t take up much PCBs, thus dairy from grazing animals tends to contain less PCBs than fish.

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Reduce Phthalate, BPA, PCB, and Pesticide Exposure

- Removing fat and skin and not frying fish may help, as PCBs accumulate in fatty tissue.
- Eat unpackaged, unprocessed whole foods.
- Use fresh and frozen fruits and veggies.
  - Plastic bags used for frozen produce don't contain phthalates and bisphenols.
- Wash fruits and vegetables before consumption.
- Limit fast food and processed meals (mac & cheese in a box, spaghetti in a can, etc.).
- Use reusable produce bags, not plastic.

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Callahan, Alice. The New York Times, 17 Apr. 2020, https://www.nytimes.com/article/plastics-to-avoid.html.

Reduce Phthalate, BPA, PCB, and Pesticide Exposure

Consider:

- Buy soups, sauces, and beverages in glass. Store food in glass.
- Especially avoid plastics with recycle numbers 3, 6 & 7.
- Avoid plastic wrap, consider beeswax wraps instead.
- Swap out your vinyl shower curtain for a fabric one.
- Avoid heating up plastics.
- Avoid touching store receipts (BPA).

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Callahan, Alice. The New York Times, 17 Apr. 2020, https://www.nytimes.com/article/plastics-to-avoid.html.

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Reduce Phthalate, BPA, PCB, and Pesticide Exposure

Consider:

- Avoid products with “fragrance”
- “unscented” products might still contain fragrance chemicals to hide other smells!
- Avoid (clean up often) dust! Phthalates can accumulate in the dust in your home.
- Use a vacuum with a HEPA filter.
- Use an air purifier indoors.
- Get rid of air fresheners!
- Replace skincare, haircare, household cleaners, etc. with EWG-certified products https://www.ewg.org/skindeep/

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Callahan, Alice. The New York Times, 17 Apr. 2020, https://www.nytimes.com/article/plastics-to-avoid.html.

Reduce Phthalate, BPA, PCB, and Pesticide Exposure

- EWG 2022 Dirty Dozen List

https://www.ewg.org/foodnews/dirty-dozen.php

Did you know?
The “Dirty Dozen” and “Clean 15” EWG lists are based on the USDA’s pesticide analyses which are not comprehensive. USDA does not test for glyphosate, for example, and rotates the fruits and veggies it tests each year.

Reduce Phthalate, BPA, PCB, and Pesticide Exposure

- EWG 2022 Clean Fifteen List

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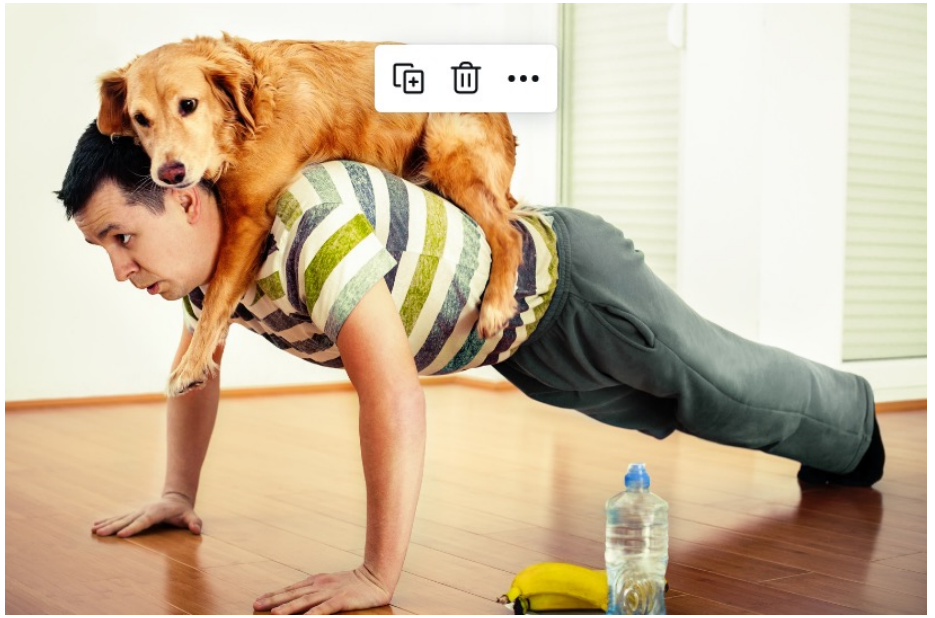
https://www.ewg.org/foodnews/clean-fifteen.php

Encourage Things That Decrease Risk

Summary of Functional Medicine Treatment Considerations

- High physical activity
- Green vegetables
- Fruit (especially citrus fruits)
- Vitamin A from animal sources
- Dairy (2009 large prospective study of black women)



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Summary of Functional Medicine Treatment Considerations

Summary of Functional Medicine Treatment Considerations

LOWER ELEVATED ESTROGEN

- Contributors to elevated estrogen include being overweight, diabetes/blood-sugar dysregulation, PCOS, perimenopause, thyroid issues, increased aromatase, EDCs, alcohol, suboptimal liver clearance, gut dysbiosis, HRT supplementation, elevated androgens, low SHBG, inflammation, stress, ovarian cysts.

ESTROGEN DETOX SUPPORT

- Diindolylmethane (DIM), indole-3-carbinol (I3C), and calcium-d-glucurate – note that these can lower estrogen levels.
- Cruciferous vegetables, apiaceae (carrot) family vegetables, rosemary, turmeric/curcumin, sulforaphane/glucoraphanin, resveratrol, glutathione, N-acetyl-cysteine (NAC), magnesium, B vitamins, choline, trimethylglycine (TMG), methionine, SAMe.

LOWER ELEVATED ANDROGENS

- Contributors to elevated estrogen include being overweight, insulin resistance/ blood-sugar dysregulation, PCOS, thyroid issues, slow aromatase, EDCs, alcohol, nicotine, suboptimal liver clearance, gut dysbiosis, HRT supplementation, low SHBG, inflammation, stress, & NCAH.

LIVER SUPPORT

- Inositol, choline, B vitamins, NAC, ALA, milk thistle, dandelion, beets, etc.

HPA-AXIS SUPPORT

- B-vitamins, vitamin C, adaptogenic herbs, stress reduction, blood sugar regulation, improving sleep, etc.

OTHER

- Melatonin, iodine, EGCG, antioxidants, probiotics, sufficient calcium, tomatoes (lycopene), cinnamon, black cohosh, castor oil.

LOWERING 16-OH-E1

- Avoid St. John's work, caffeine, smoking, alcohol, PAHs, pesticides
- Lose weight, if appropriate
- Improve sulfation: NAC, MSM, sulforaphane, taurine, methionine, glutathione, sulfurous foods, molybdenum
- Improve glucuronidation: sulforaphane, citrus fruits, quercetin, curcumin, calcium-d-glucurate
- CYP3A4 inhibitors (inhibit at your own risk!): grapefruit, resveratrol, rosemary, wild yam, peppermint oil
- Encourage the 2-OH pathway: cruciferous vegetables, apiaceae (carrot) family vegetables, rosemary, fish oil, soy, flaxseeds, and avoiding a high sugar diet and alcohol.

DISCOURAGE THINGS THAT INCREASE RISK

- Phthalates, BPA, PCBs, pesticides, alcohol, food additives, caffeine (weak association), red meats and ham, omega-3s from unreputable sources, OCPs at an early age (13-16 yo), chronic stress, vitamin D deficiency, obesity, and high blood pressure.

ENCOURAGE THINGS THAT DECREASE RISK

- Vitamin A, dairy, green vegetables, fruit (especially citrus), high physical activity.

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One More Study!

Dietary Natural Compounds and Vitamins as Potential Cofactors in Uterine Fibroids Growth and Development

Nutrients. 2022 Feb 9;14(4):734. doi: 10.3390/nu14040734.

Abstract

An analysis of the literature generated within the past 20 year-span concerning risks of uterine fibroids (UFs) occurrence and dietary factors was carried out. A link between Vitamin D deficiency and UFs formation is strongly indicated, making it a potent compound in leiomyoma therapy. Analogs of the 25-hydroxyvitamin D3, not susceptible to degradation by tissue 24-hydroxylase, appear to be especially promising and tend to show better therapeutic results. Although research on the role of Vitamin A in the formation of fibroids is contradictory, Vitamin A-enriched diet as well as synthetic retinoid analogues, may be preventative or limit the growth of fibroids. Unambiguous conclusions cannot be drawn regarding Vitamin E and C supplementation, except for alpha-tocopherol. Alpha-tocopherol as a phytoestrogen taking part in the modulation of estrogen receptors (ERs) involved in UF etiology, should be particularly avoided in therapy. A diet enriched in fruits and vegetables, as sources of carotenoids, polyphenols, quercetin, and indole-3-carbinol, constitutes an easily modifiable lifestyle element with beneficial results in patients with UFs. Other natural substances, such as curcumin, can reduce the oxidative stress and protect against inflammation in leiomyoma. Although the exact effect of probiotics on uterine fibroids has not yet been thoroughly evaluated at this point, the protective role of dairy products, i.e., yogurt consumption, has been indicated. Trace elements such as selenium can also contribute to antioxidative and anti-inflammatory properties of a recommended diet. In contrast, heavy metals, endocrine disrupting chemicals, cigarette smoking, and a diet low in antioxidants and fiber were, alongside genetic predispositions, associated with UFs

This 2022 study mentions a lot of what we've already talked about!

- Encourages vitamin D3, vitamin A, fruits, vegetables, carotenoids, polyphenols, quercetin, indole-3-carbinol (I3C), curcumin, dairy products, selenium.
- Discourages heavy metals, endocrine disrupting chemicals (EDCs), cigarette smoking, diet low in antioxidants and fiber, alpha-tocopherol.

Szydłowska I, et al. Nutrients. 2022 Feb 9;14(4):734.

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