

Estrogen Metabolism in Males

Importance of Estrogen Detoxification

- Healthy estradiol metabolism and clearance is important for regulating estradiol levels and reducing male cancer risk (e.g., prostate cancer).
- Elevated estradiol in males has been associated with breast tissue enlargement, obesity, mood changes, low sex drive, and impaired erectile function.
- Because testosterone aromatizes to estradiol, when using testosterone replacement therapy (TRT) or any other therapies that can increase testosterone levels (clomiphene, hCG, etc.) it is important to ensure that estrogen is being appropriately cleared out of the body.

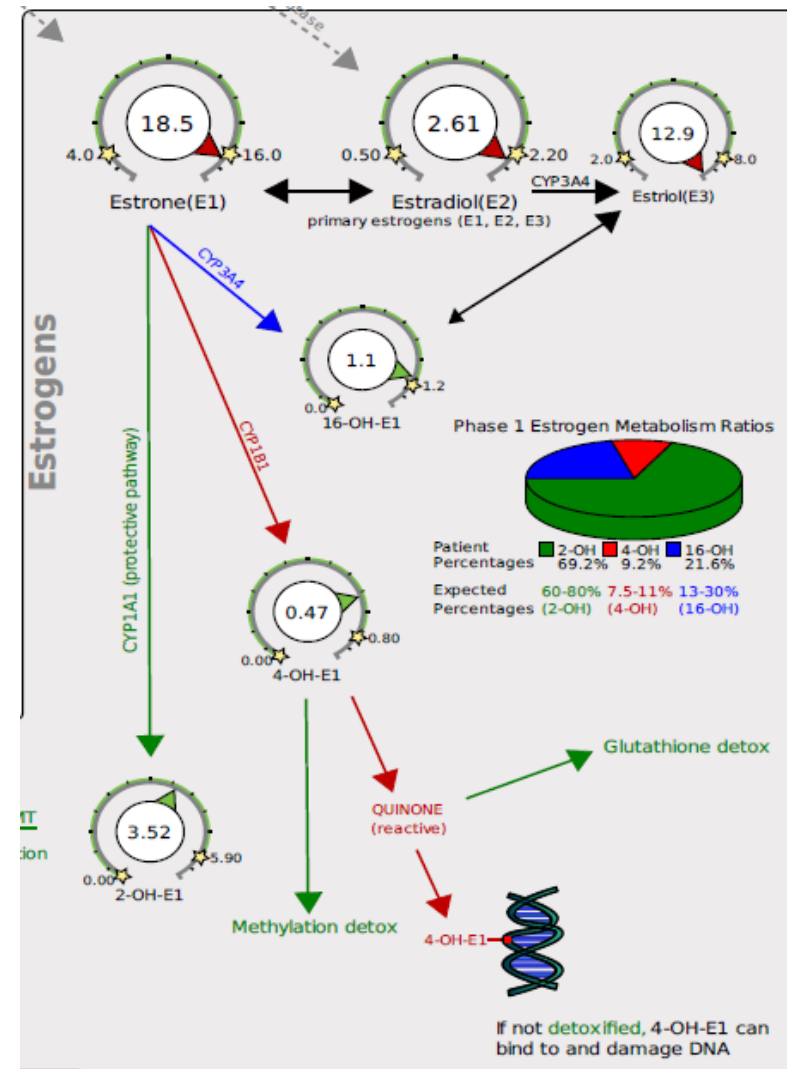
Phase 1 Estrogen Detox

Phase 1 Estrogen Detox

In phase 1, estrone (E1) and estradiol (E2) are hydroxylated into:

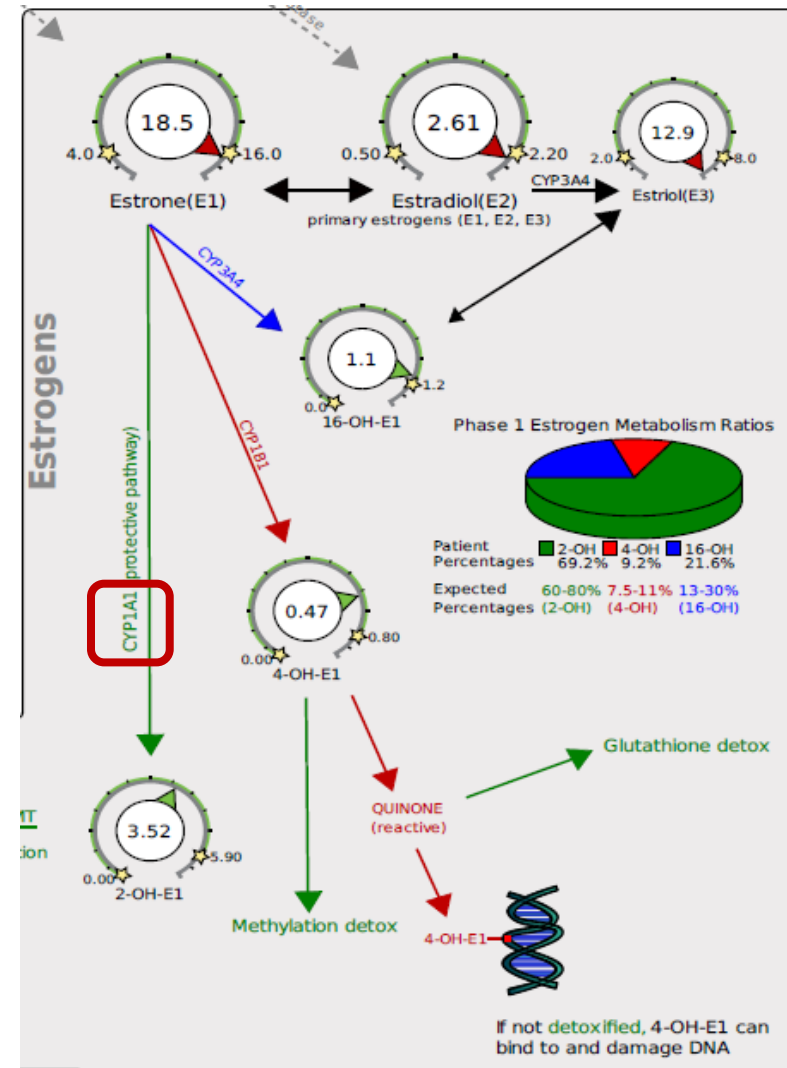
- 2-hydroxy (2-OH) metabolites
- 4-hydroxy (4-OH) metabolites
- 16-hydroxy (16-OH) metabolites

These intermediate metabolites can cause oxidative damage in the body. Thus, they require further processing in phase 2 to be turned into more stable compounds that are ready for elimination.

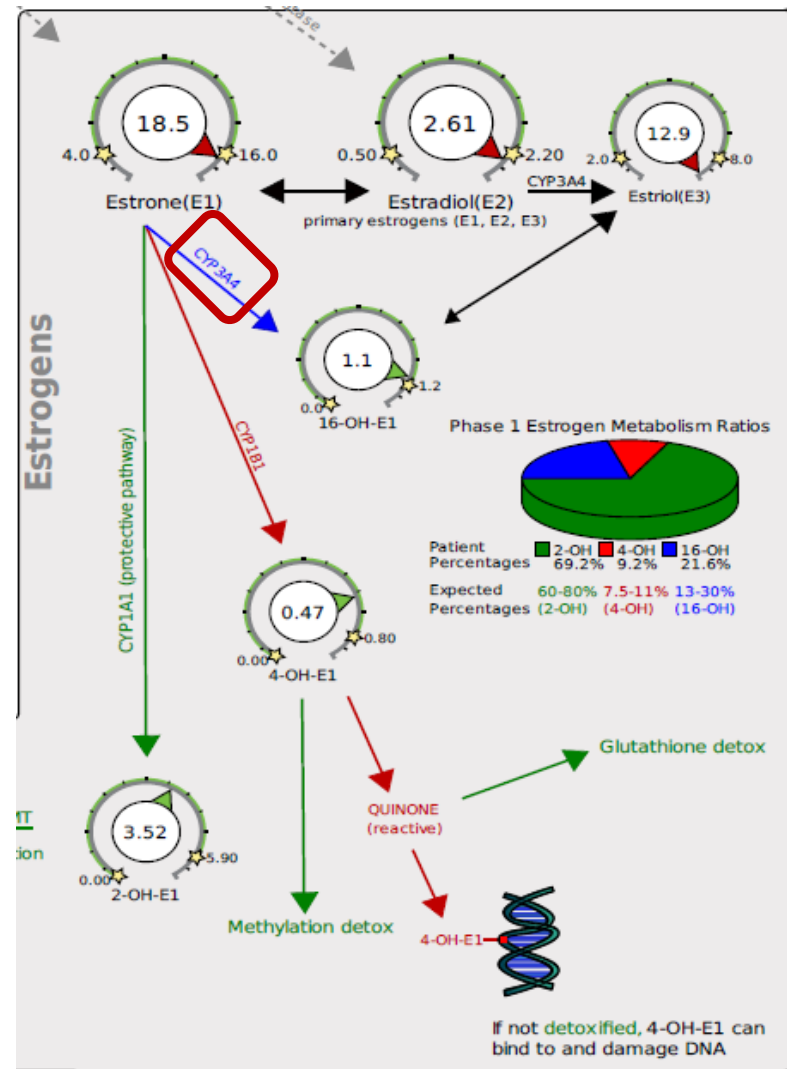


Phase 1 Estrogen Detox

- **CYP1A1** is the enzyme responsible for converting E1 to **2-OH-E1** and E2 to **2-OH-E2**.
- This is the “preferred pathway” because 2-OH metabolites are the most stable of the three phase 1 estrogen metabolites measured on the DUTCH test.

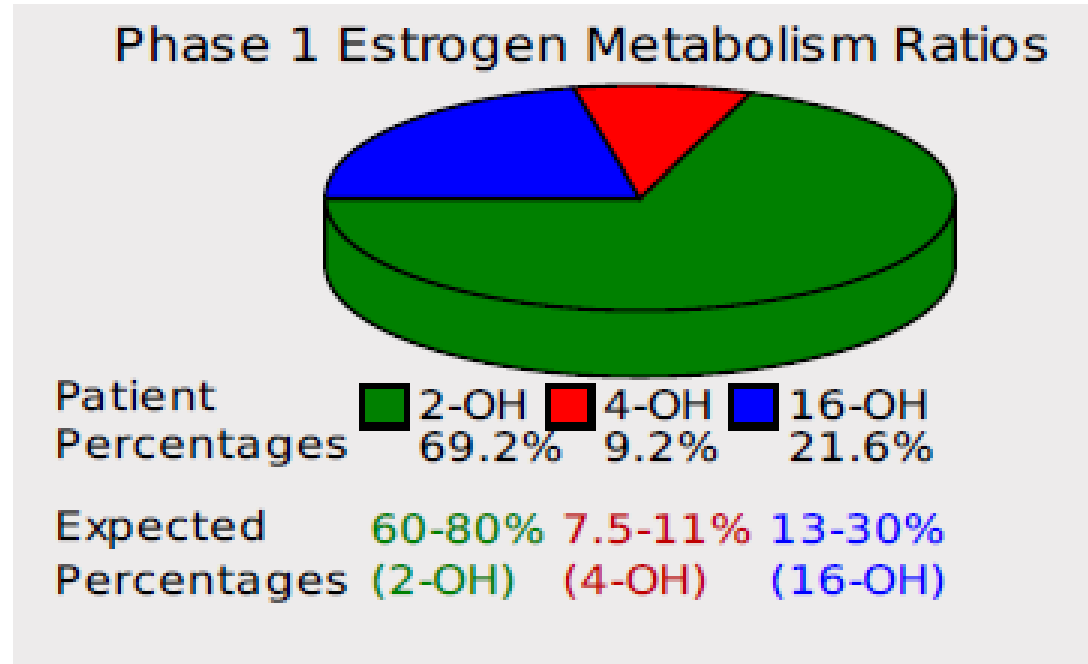


Phase 1 Estrogen Detox



- **CYP3A4** is the enzyme responsible for converting E1 to **16-OH-E1**, and E2 to **16-OH-E2 (estriol)**.
- 16-OH-E1 is a proliferative estrogen, although less estrogenic than estradiol (E2).
- Elevations in 16-OH-E1 may exacerbate estrogen excess symptoms and can contribute to estrogen sensitive tissue proliferation (prostate issues, etc.).
- However, 16-OH-E1 may be beneficial for bone health so low levels in the context of low estradiol (E2) may be concerning.

Phase 1 Estrogen Detox

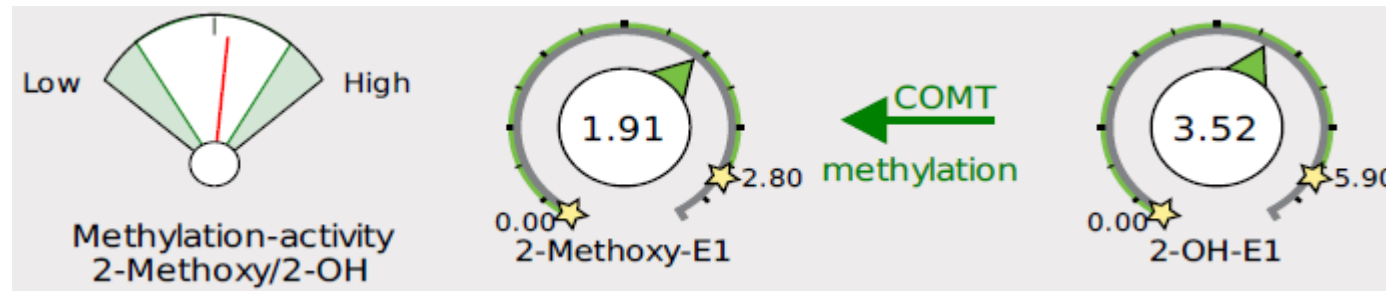


- The pie chart on page #3 of the DUTCH Complete and DUTCH Plus reports shows the relative ratios of the three phase 1 metabolites.
- Ensure that the 2-OH percentage is above 60%, the 4-OH percentage is below 11% and the 16-OH percentage is below 30%.
- Note that if estrogen metabolite levels are very low, maintaining these specific percentages may be less important.

Phase 2 Estrogen Detox

Phase 2 Estrogen Detox

- In phase 2, the phase 1 estrogen metabolites are turned into more stable compounds. Adequate methylation activity is important for converting the reactive phase 1 (especially 4-OH) estrogen metabolites into inactive phase 2 estrogen metabolites that can no longer damage DNA.
- The “methylation-activity” fan gauge estimates COMT activity by showing the patient's ratio of 2-Me-E1 to 2-OH-E1. Ideally the 2-methoxy-E1 result will be at least $\frac{1}{2}$ of the 2-OH-E1 result.



- The DUTCH test does not assess total body methylation activity; however, the DUTCH test may help identify those patients who may have decreased or increased methylation activity.

Phase 3 Estrogen Detox

Phase 3 Estrogen Detox

- In phase 3, estrogens are eliminated in the bile (stool) and urine.
- The DUTCH test does not include any direct phase 3 estrogen detoxification markers, however it does include indican which, when elevated, is a marker of bacterial overgrowth and dysbiosis in the gut.
- Indican may be a useful marker when investigating contributors to estrogen excess, as gut health is important for maintaining healthy levels of estrogen in the body.

Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)

Indican

Within range

Key Points

- Healthy estrogen metabolism and clearance is important for regulating estradiol levels and reducing male cancer risk (e.g., prostate cancer).
- Estrogen goes through three detox phases. The DUTCH Test measures five phase 1 metabolites and one phase 2 metabolite.
- It is ideal if most estrogen is metabolized into the 2-OH metabolites, as these are the most stable. The 4-OH metabolites are the most genotoxic (can damage DNA).
- Adequate methylation activity in phase 2 is important for converting the reactive phase 1 (especially 4-OH) estrogen metabolites into inactive phase 2 estrogen metabolites that can no longer damage DNA.
- In phase 3, estrogens are eliminated in the bile (stool) and urine. The DUTCH test does not include any direct phase 3 estrogen detoxification markers, however it does include indican which, when elevated, is a marker of bacterial overgrowth and dysbiosis in the gut.

References

- Cavalieri EL, Rogan EG. Depurinating estrogen-DNA adducts in the etiology and prevention of breast and other human cancers. *Future Oncol.* 2010 Jan;6(1):75-91. doi: 10.2217/fon.09.137. PMID: 20021210; PMCID: PMC4422115.

Thank You!

If you are interested in learning more about hormones, each week we hold one-hour long mentorship sessions! Once you are a registered DUTCH provider, you can book these through our online scheduling link. Please call to get registered today.

For questions, contact:

info@dutchtest.com

(503) 687-2050

www.dutchtest.com

