

The HIT Test in Practice: Understanding Oestrogen Metabolism

Charlotte Hunter
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Meet the Team



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Overview

- The Hormone Insights Test (HIT)
- Oestrogen basics
- Steroid pathways*
- Oestrogen metabolism overview
- Methylation
- BPA
- What next?



There IS Another Way!



- The Hormone Insight Test (HIT): Powered by the *Advanced Urine Hormone Metabolites Test by ZRT*
- Measures **44 hormone-related markers**
- 13 oestrogens, 8 androgens
- Diurnal cortisol & melatonin patterns
- Includes **BPA** (rarely assessed endocrine disruptor)

The Hormone Insights Test (HIT)



- Developed by ZRT laboratory – pioneers in hormone testing
- The **ORIGINAL** urine metabolites test
- Built on decades of research and clinical use
- The HIT Test combines ZRT's scientific credibility with KBMO's practitioner-first support model.



Oestrogen Basics



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Why assess oestrogen metabolism?

- Reveals metabolism pathways and patterns
- Links results to symptoms and/or history
- Assess hormone-responsive cancer risk
- Useful pre-HRT baseline
- Relevant in autoimmune disease



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Oestrogen basics: where is it made?

- Ovarian granulosa cells (primary source, and most well know)
- Adipose tissue
- Skin fibroblasts
- Bone
- Brain
- Placenta
- ...almost everywhere!



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Tissue targets

- Acts on every cell in the body
- Influences gene transcription
- Works via nuclear & membrane receptors
- Explains wide range of symptoms in menopause



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Actions of oestrogen

- Modulates **inflammation**
- Regulates **cell proliferation & differentiation**
- Influences **angiogenesis**
- Supports **bone health**
- Governs **ovulation & reproduction**
- Provides **neuroprotection** (key in menopause research)



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**Oestrogen is a
powerful modulator,
but only if it is present
in the right place, at
the right time, and in
the right amounts!**

Steroid Pathways



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The Parent Oestrogens

- **Oestriol (E3):** weakest, lowest receptor binding ($\sim 1/10$ of E2)
- **Oestradiol (E2):** most potent; postmenopausal elevations may increase risk in some contexts
- **Oestrone (E1):** converts to E2, E1-S, or metabolites; often elevated in PCOS



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Oestrogen Metabolism



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Oestrogen metabolism

- Looks complex at first – focus on the big picture
- 3 main cytochrome enzymes:

CYP3A4 → Oestriol (E3)

CYP1A1 → Oestrone (E1) & Oestradiol (E2)

CYP1B1 → Oestrone (E1) & Oestradiol (E2)

- COMT methylates catechol oestrogens (from CYP1A1 & CYP1B1)
- Metabolites are excreted in urine or stool

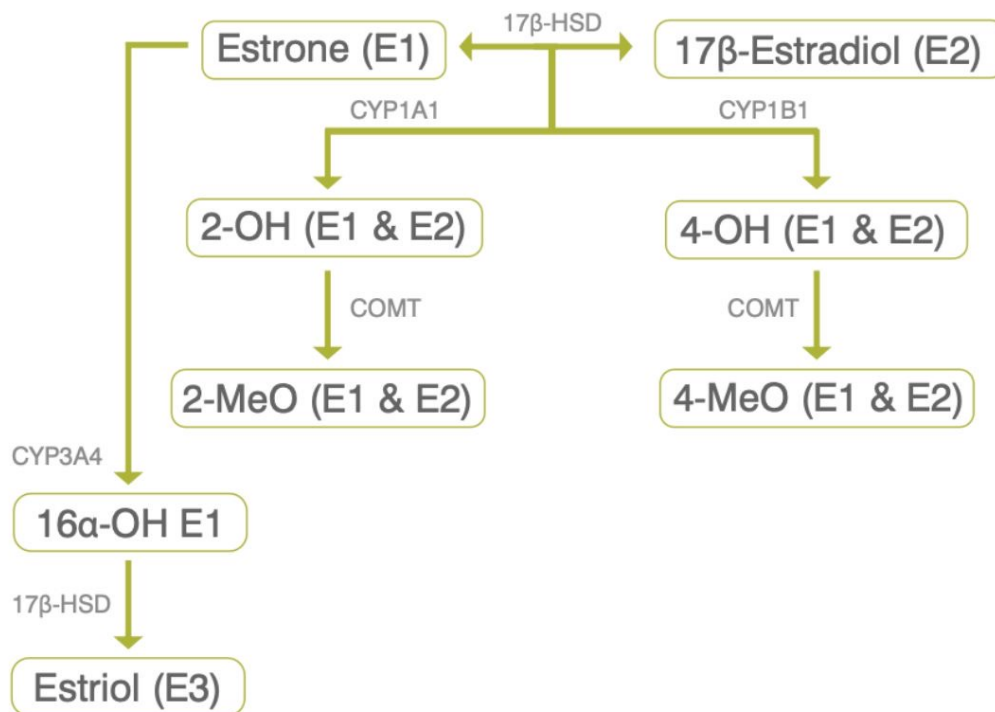


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Oestrogen Quotient (EQ)

- $EQ = E3 \div (E2 + E1)$
- Ratio >1 = optimal
- Described by Henry Lemon: higher EQ linked to better breast cancer survival
- ZRT observation: low EQ sometimes seen with low iodine status (not diagnostic)

Steroid Hormone Cascade



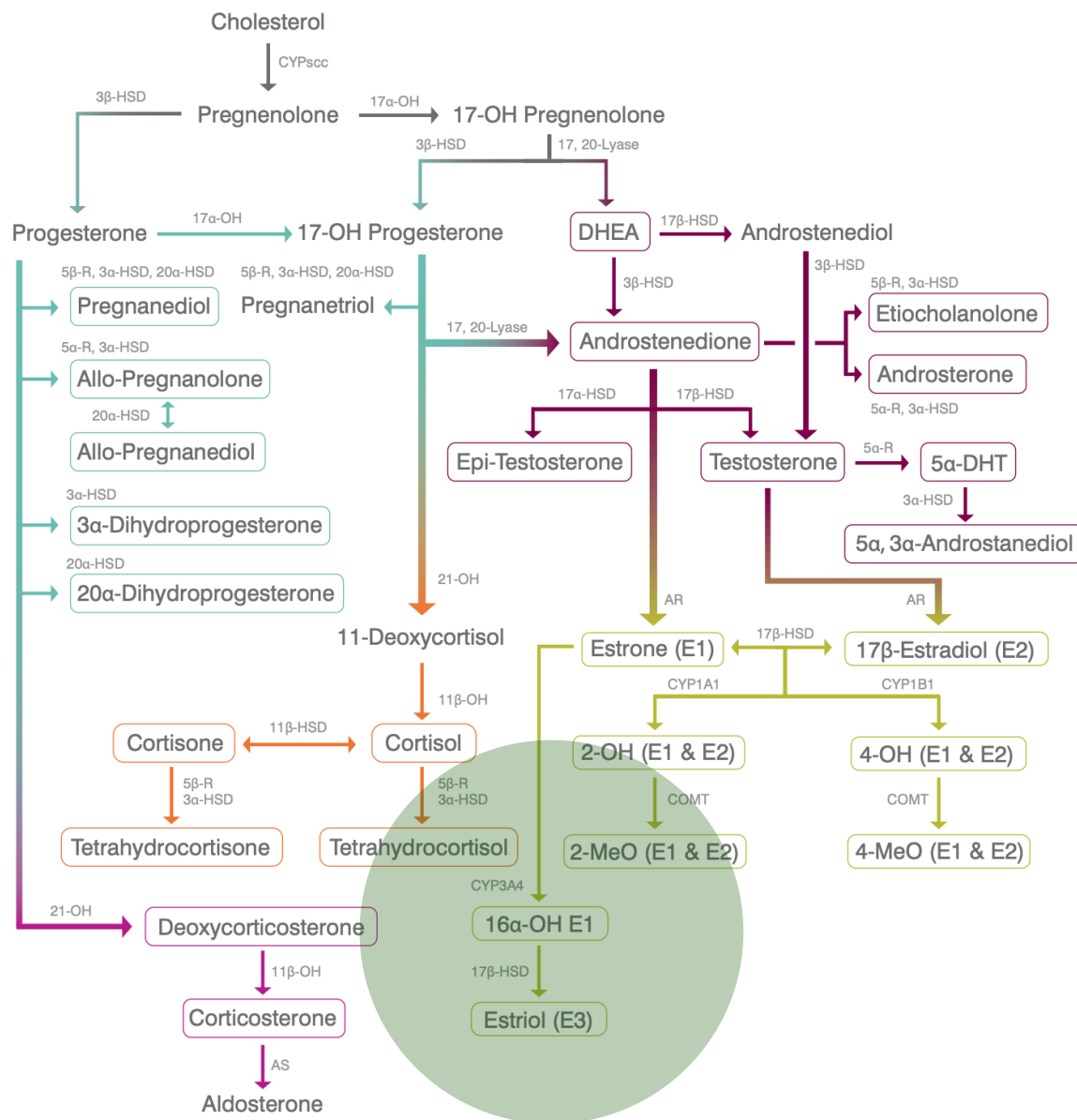
- Aromatase → E1 & E2
- E1 ↔ E2 via 17β-HSD (type 1 & 2)
- E1 → 16-OH-E1 → E3 (CYP3A4)
- E1 & E2 → CYP1A1 / CYP1B1 → catechol metabolites → DNA adduct risk
- COMT methylation = protection



16-OH E1



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(11β-HSD) 11β-Hydroxysteroid dehydrogenase
 (17α-HSD) 17α-Hydroxysteroid dehydrogenase
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 (COMT) Catechol-O-Methyl-Transferase

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 17,20-Lyase (same enzyme as 17α-OH)
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- Androgens
- Estrogens
- Glucocorticoids
- Mineralocorticoids
- Progestogens



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CYP3A4

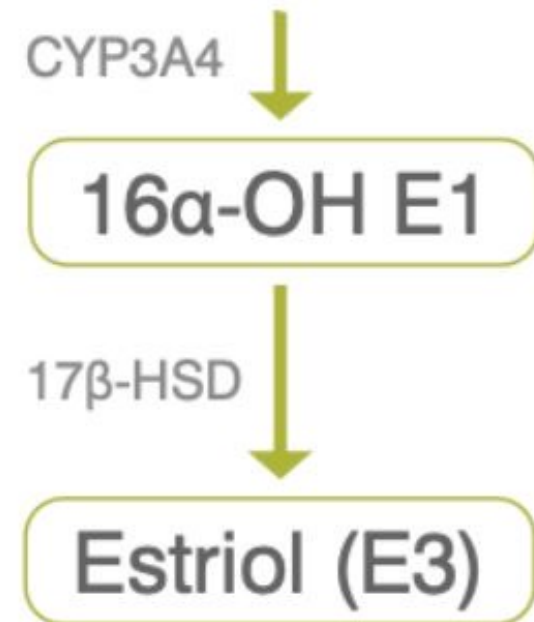
- Handles many substrates – highly active enzyme
- Overactivity → ↑ 16-OH-estrone
- Impacted by lifestyle, diet, meds, supplements
- Many inhibitors & inducers (check reliable sources)



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16-OH E1

- Post-menopause: supportive for bone & blood pressure
- Pre-menopause: proliferative, ↑ cancer risk, ↑ inflammation
- Context-dependent – interpretation varies



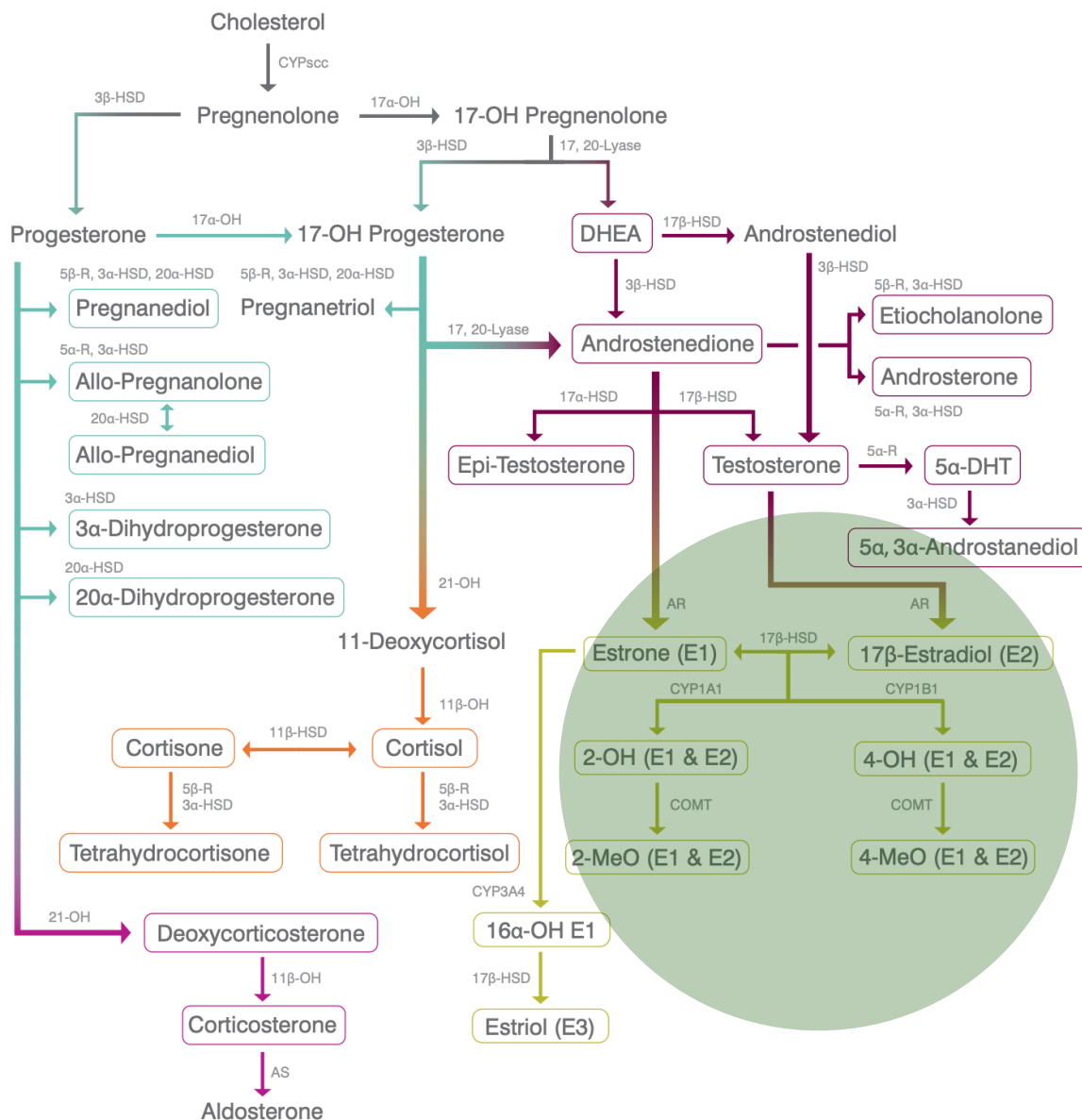
CYP3A4 & 16-OH E1

Increased by:

- Smoking
- Caffeine
- BPA
- St John's Wort
- Pesticides
- PAHs
- Alcohol (even moderate)
- Obesity

Decreased by:

- Grapefruit
- Resveratrol
- Rosemary
- Wild yam
- Peppermint oil
- Curcumin (mild inhibition)
- Azole antifungals
- Some antibiotics



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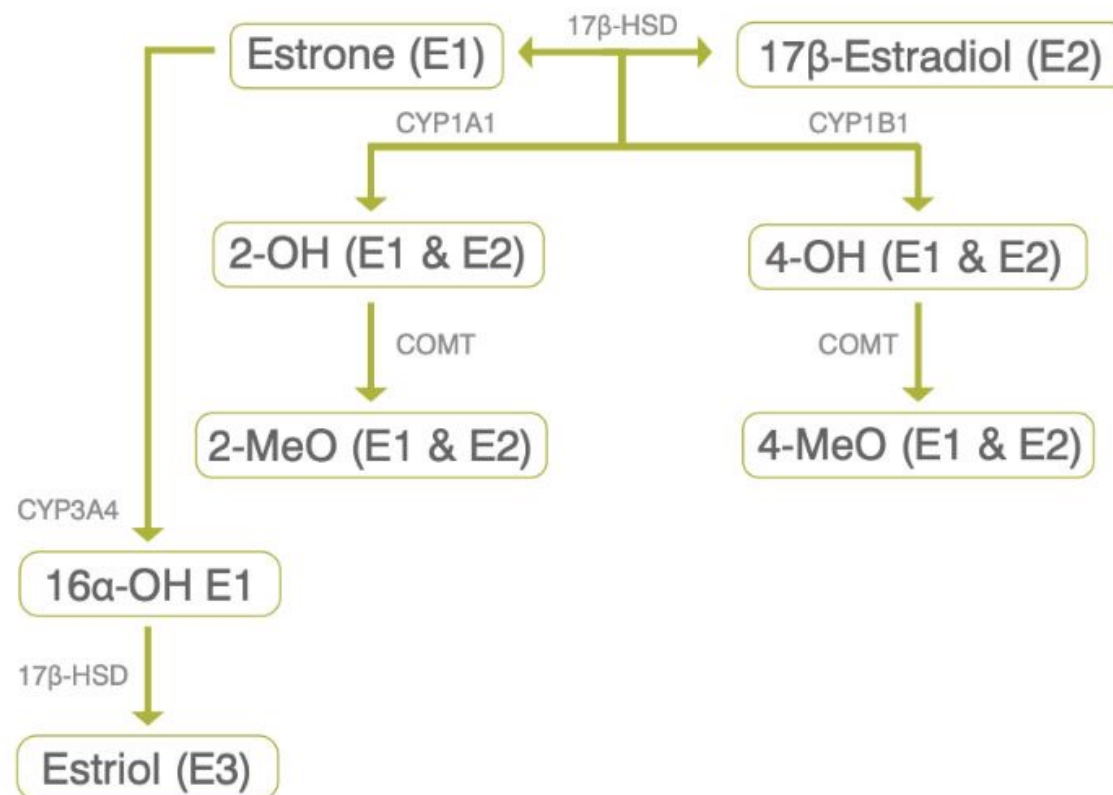
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CYP1A1 & CYP1B1



CYP1A1 & CYP1B1

- Both → catechol oestrogens
- CYP1A1 → 2-OH (safer pathway)
- CYP1B1 → 4-OH (riskier pathway)
- Catechols → quinones → potential DNA damage
- Influenced by genetics + lifestyle



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2-OH E1 & E2



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CYP1A1 (the “2s”)

Good:

- Protective
- Weaker activity
- Less carcinogenic
- Less proliferation
- Induces apoptosis

Bad:

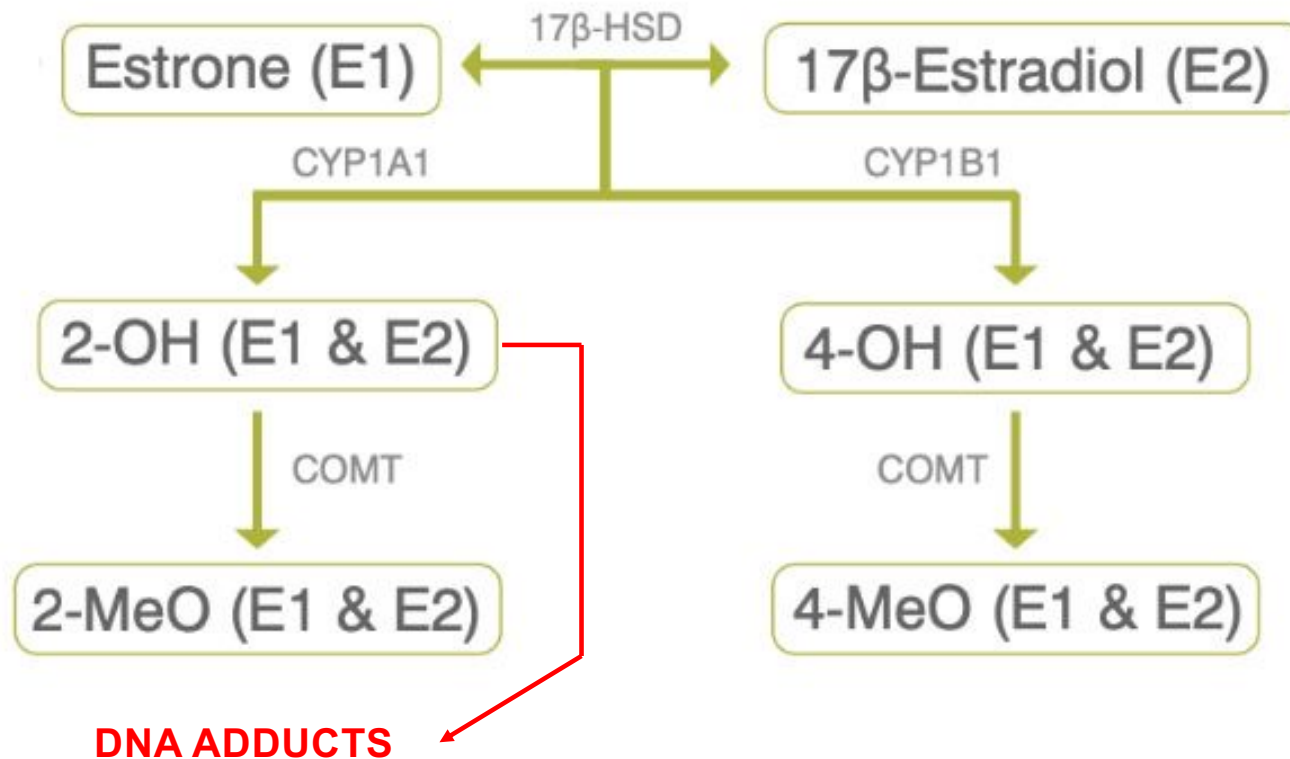
- High levels may be associated with endometrial cancers
- Higher in AI (e.g. RA or SLE)
- Can form quinones if not methylated

*Take-home: The 2s are not a free pass!
Good or bad? Depends on context*



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2-OH E1 & E2



Supporting CYP1A1 & “the 2s”

Speeds up:

- Cruciferous vegetables
- Flax
- Fish oils
- Soya
- Rosemary
- Thyroxine

Slows down:

- Coffee
- Smoking
- Alcohol
- High sugar diet
- Resveratrol

Clearance is also important (COMT/methylation)

Detox, methyl donors and gut health (FIT Test & Gut Barrier Panel)



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4-OH E1 & E2



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CYP1B1 & “the 4s”

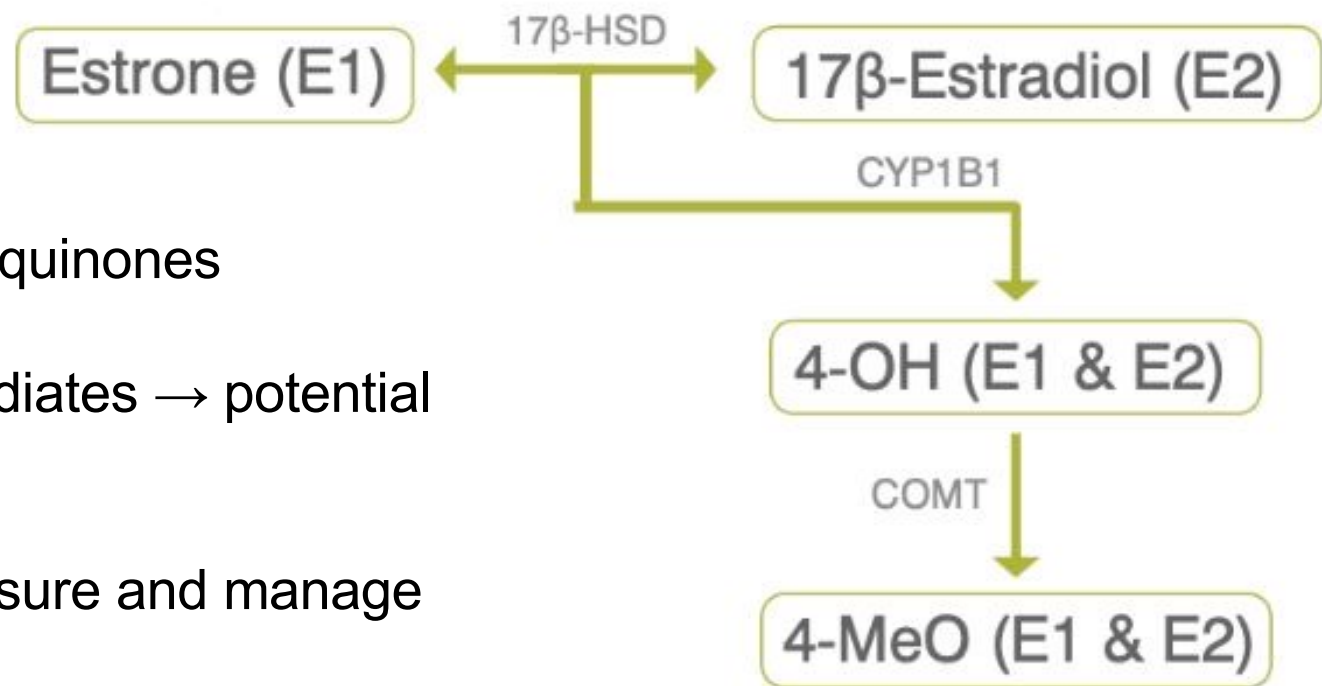
- Proliferative, anti-apoptotic
- Higher activity in pregnancy and myometrium
- Prefers E2 > E1 (higher affinity)
- Can form DNA adducts under oxidative stress
- Binds to oestrogen receptors



*Is it being
cleared?*

4-OH E1 & E2

- Can form E2-3,4 quinones
- Reactive intermediates → potential DNA adducts
- Important to measure and manage



Methylation



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What Can Impact Methylation?

- Genetics (COMT variants)
- Co-factors: Mg, B vitamins, folate, choline, methionine, SAMe, TMG
- Medications: OCPs, diuretics, PPIs, corticosteroids, sulfonamides
- Physiology: hypochlorhydria, smoking, SAD (seasonal affective disorder)
- Enhancers: ellagic acid (berries), lithium orotate, riboflavin, lower protein



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How to Assess Methylation?

Assess the relativity of the hydroxylated intermediates to the methylated products.

HYDROXYLATION



METHYLATION



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2- & 4-MeO Products

- Produced via COMT - SNPs can limit methylation
- Products = inert / beneficial
- Key question: COMT activity?
- Support by: ↓ oxidative stress, methylation co-factors, neutralising catechols

Reducing Oxidative Stress

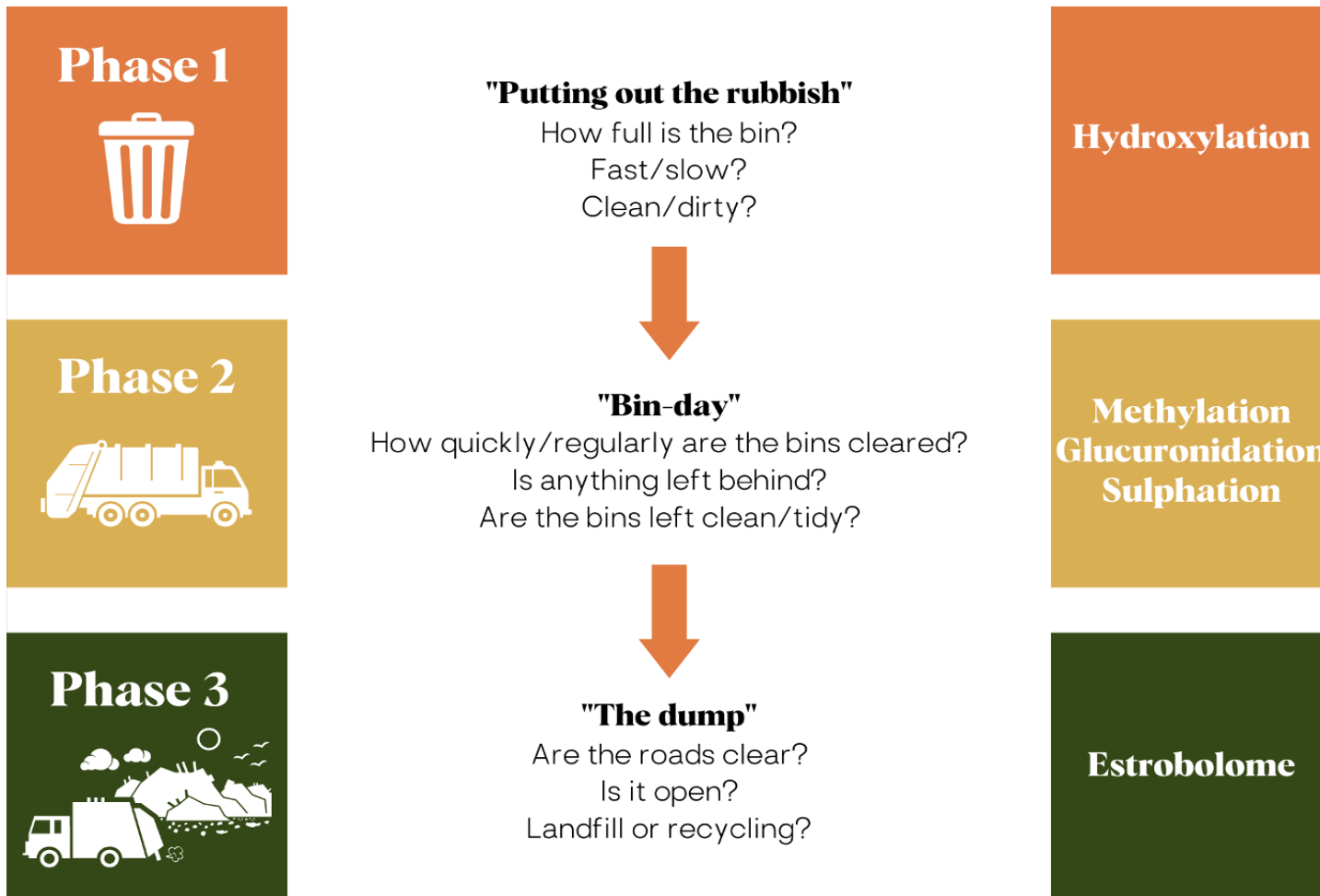
- Resveratrol
- Quercetin & bioflavonoids
- Proanthocyanidins
- Selenium
- Grape seed / pine bark extract
- Glutathione & NAC
- Avoid toxin exposure
- Aim: reduce risk

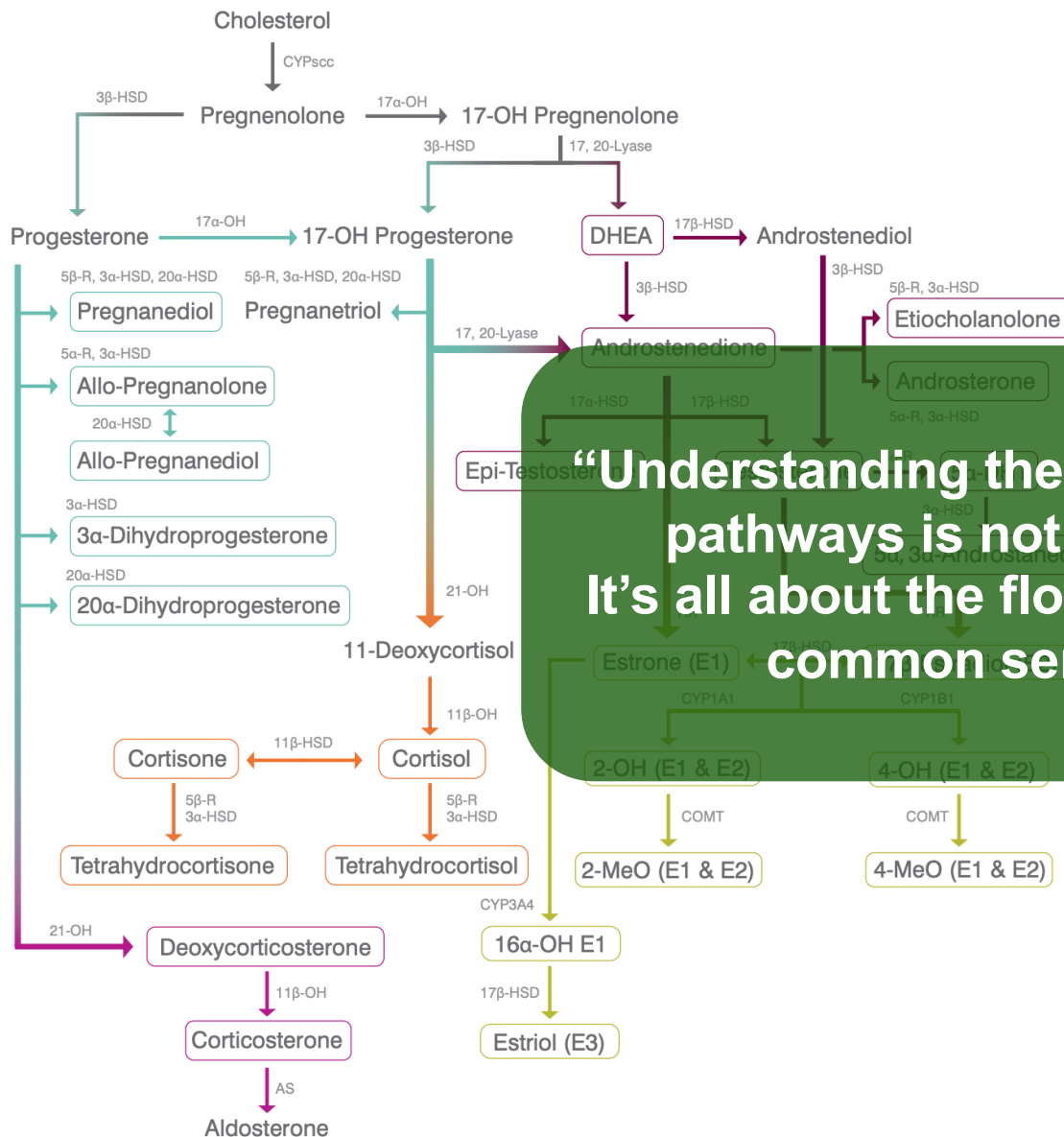


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Supporting Methylation

- Key supports: DIM, TMG, SAMe, B6, B12, folate (MTHFR), methionine, betaine, magnesium
- More methylation $\neq$ better
- Always monitor client symptoms (e.g. wired, overstimulated)





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“Understanding the steroidogenic pathways is not a dark art! It's all about the flow, with a bit of common sense...”

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Bisphenol-A



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Bisphenol-A

- Suppresses methylation
- Potent endocrine disruptor
- Binds oestrogen receptors → proliferation signaling
- Implicated in in utero effects
- Linked to cancers
- Found in plastics, till receipts, can linings
- Hard to avoid – use vigilance & common sense



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What's Next?



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Dr Shania Seeber

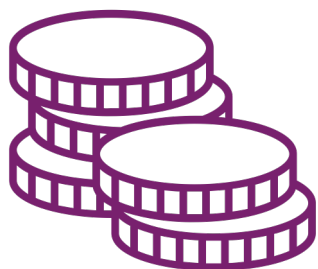
The image shows three overlapping presentation slides for the Hormone Insights Test (HIT). The top-left slide is titled "Hormone Insights Test (HIT) - DISCOVER THE ZRT DIFFERENCE" and includes the text "Introducing ZRT's Hormone Metabolites Test: Powerful, Precise, Practical" along with the KBMO and ZRT logos. The top-right slide is titled "Hormone Insights Test (HIT) - the importance understanding hormone metabolites" and includes the text "Understanding the Analytes and Actioning on them" along with the KBMO and ZRT logos. The bottom slide is titled "Case study using the HIT test Hormone Insights Test" and includes the text "Introducing ZRT's Hormone Metabolites Test: Powerful, Precise, Practical" along with the KBMO and ZRT logos. All slides feature a background graphic of a stylized green leaf and a red cross.

Hormone Insights Test (HIT) - DISCOVER THE ZRT DIFFERENCE
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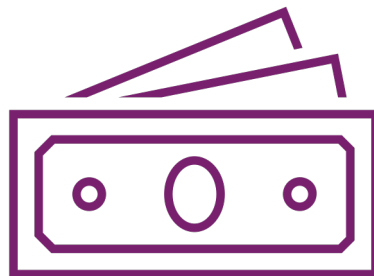
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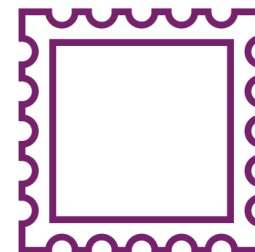
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Practitioner Price
£249



Retail Price
£299



FREE Postage
& Returns

Your Next Steps with HIT

- Order your first test at www.kbmodiagnostics.co.uk
- Attend your first 1:1 session
- Bring your cases and questions to the Hormone Help Hour
- Enjoy the 3 brilliant webinars with Dr Shania Seeber to build your knowledge on the HIT.

Stay in Touch



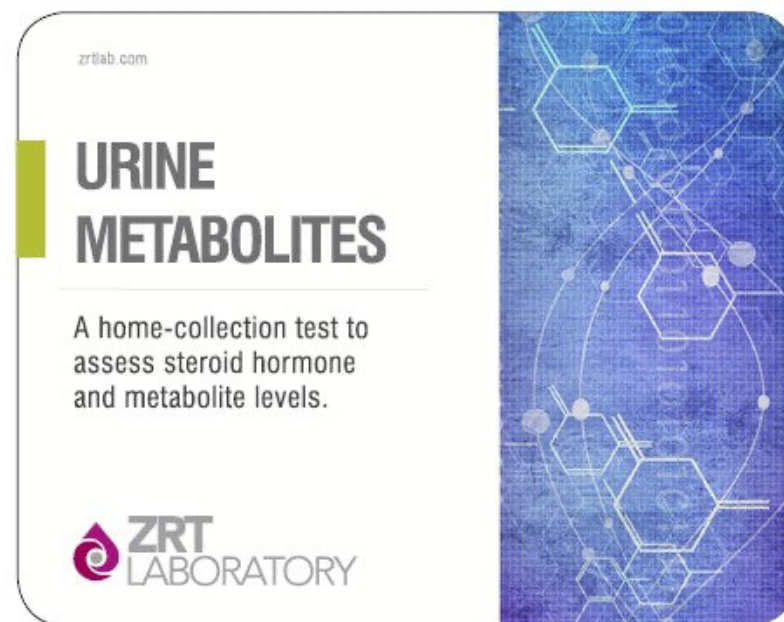
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Thank You



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